



MCEM Part A Course

April 26th - 27th 2014

Chennai, India



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Please note that after the course you will be emailed a link to access a selection of videos showing MCEM Part A lectures from a previous course



MCEM(UK) Part A Exam Preparation Course

GAMET 2014: Global Health City, Chennai

Saturday 26th April –Sunday 27th April 2014

Saturday April 26th

08.30	<i>Course Registration & welcome</i>	
09.00	Introduction to the course	Dr I Stell & Dr M Hall
09.10	Full MCEM A practice paper : Paper I	
10.10	Marking Paper I	Dr M Hall
10.30	Exam & revision tips	Dr M Hall
11.00	<i>Coffee</i>	
11.20	Microbiology	Dr I Stell
12.10	Respiratory physiology	Dr J Thiagarajan
13.00	<i>Lunch</i>	
14.00	Short practice paper : Clinical questions	
14.20	Marking short paper and discussion	Dr Kotamraju
15.00	Pathology	Dr M Hall
15.40	<i>Tea</i>	
16.00	Haematology	Dr C Trivedy
16.45	Neuroanatomy and physiology	Dr M Hall
17.30	<i>Feedback/close</i>	Faculty

Sunday April 27th

09.00	<i>Introduction to the day</i>	
09.05	Full MCEM A practice paper : Paper II	
10.00	Marking Paper II	Dr C Trivedy
10.15	Cardiovascular physiology	Dr M Hall
11.00	Pharmacology I	Dr I Stell
11.30	<i>Coffee</i>	
11.45	Pharmacology II	Dr I Stell
12.30	Short Practice Paper : Frequently asked questions	
12.45	Marking short paper and discussion	Dr M Hall
13.15	<i>Lunch</i>	
14.15	Anatomy I (upper limb, head & neck)	Dr C Trivedy
15.15	Working in the UK: the MTI Programme	Dr J Thiagarajan
15.45	<i>Tea</i>	
16.00	Anatomy II (lower limb, chest & abdo)	Dr J Thiagarajan
16.45	MCEM Quiz	Dr M Hall
17.30	<i>Concluding remarks and close</i>	Faculty

Part 1

Exam Tips and Revision



MCEM Part A: Exam Tips and Revision

"Exam designed to allow the candidate to demonstrate their knowledge and understanding of the application of the key basic sciences to emergency medicine."

The exam : 50 questions
 4 parts
 T/F each
 No negative marking
 2 hours (enough time for most)

The Questions : It is an exam oriented around key topics in the basic sciences

Read each question carefully
 Most straightforward
 Few have a brief clinical scenario
 no 'trick' questions

They do not stray from the curriculum!

Are the questions in the course practice exams representative? YES!

mostly basic sciences with a few clinical 'emergency medicine' Qs
 some 'ambiguity' in questions is unavoidable

Distribution of Questions between Domains

	College advise	Rough average of past exams
Anatomy	10 questions	12
Patho-physiology	10	11
Pharmacology	5	5
Microbiology	5	6
Pathology	2-3	3
Haematology	5	2-3
Clinical chemistry	5	2-3
Statistics/EBM	2-3	2
Emergency medicine	5	5-6



Curriculum :

Found on College Emergency Medicine Website
 Appendix 7 : Basic Sciences Curriculum June 2010
 Excellent resource and guide for revision – **USE IT!**

Revision books :

- Physiology at a Glance (Ward, Clarke and Linden, Blackwell Science 2004)
- Basic Medical Sciences for MRCP 1 (Phillipa Easterbrook, Churchill Livingstone)
- Revision notes for MCEM Part A (Mark Harrison, Oxford Specialty Training)
- Oxford Handbook of Medical Sciences (Wilkins et al, Oxford Medical Publishers)
- Oxford handbooks, A&E, Clinical medicine, Specialties (for clinical stuff)
- Applied Basic Science for Basic Surgical Training (Raftery, Churchill Livingstone)
- Lecture Notes in Human Physiology (Bray, Blackwell)
- Clinical Anatomy (Harold Ellis, Blackwell 2006)
- Clinical Biochemistry, an Illustrated text (Gaw, Murphy and Cowan, Churchill Livingstone)
- Medical Pharmacology at a Glance (Neal, Blackwell), then syllabus and BNF

Practice Question Books

Get Through MCEM: MCQs Pt. A (Get Through Series) by I. Beardsell, S. Bell, and D. Hulbert (Paperback - 1 Aug 2009) £24.95

Practice Papers for MCEM Part A by Jaydeep Chitnis, Gary Cumberbatch, and Ananda Gankande (Paperback - 16 Oct 2009) £24.99

Clinical Anatomy MCQs (Roger Dalton, Kaird Press 2012)

Websites	MCEM.org.uk mcemcourses.org emergencymed.org.uk	list topics and 60 free MCQs our course website with many MCEM resources CEM website for exam information
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GOOD LUCK !

Part 2

Course Lectures

Microbiology Handout – April 2014

1. Curriculum (Versn June 2010 on college website)

Part A Principles of Microbiology

- Natural and innate immunity
- Mechanisms of Disease
- Controlling infection
- Principles of investigation
- Principles of immunisation

Specific pathogen groups

- Streptococci and staphylococci
- Tuberculosis
- Clostridial infection
- Neisseria
- Pertussis
- Klebsiella, salmonella, E coli
- Gram negative intestinal disease
- Legionella
- Pseudomonas
- Chlamydia
- Herpes simplex and zoster
- HIV
- Hepatitis
- Measles, mumps, rubella
- Respiratory viruses
- Gastrointestinal viruses
- Yeasts and fungi
- Worms
- Malaria

Principles of Immunisation			
Childhood schedule			
Two months old	Diphtheria, tetanus, pertussis (whooping cough), polio and <i>Haemophilus influenzae</i> type b (Hib) Pneumococcal infection	D ¹ Ta ¹ P ² /IPV ² /Hib ³ + Pneumococcal conjugate vaccine, (PCV ³), Rotarix ^{4,5}	
Three months old	Diphtheria, tetanus, pertussis, polio and <i>Haemophilus influenzae</i> type b (Hib) Meningitis C	D ¹ Ta ¹ P ² /IPV ² /Hib ³ + MenC ³ , Rotarix ^{4,5}	
Four months old	Diphtheria, tetanus, pertussis, polio and <i>Haemophilus influenzae</i> type b (Hib) Meningitis C Pneumococcal infection	D ¹ Ta ¹ P ² /IPV ² /Hib ³ + MenC ³ + PCV ³	

Around 12 months	<i>Haemophilus influenza type b</i> (Hib) Meningitis C	Hib ³ /MenC ³
Around 13 months old	Measles, mumps and rubella Pneumococcal infection	M ⁴ M ⁴ R ⁴ + PCV ³
Three years and four months or soon after	Diphtheria, tetanus, pertussis and polio Measles, mumps and rubella	D ¹ Ta ¹ P ² /IPV ² or dTa ¹ P/IPV ² +M ⁴ M ⁴ R ⁴
Thirteen to eighteen years old	Diphtheria, tetanus, polio	Ta ¹ d/IPV ²

¹toxoid, ²inactivated, ³conjugate, ⁴live, ⁵from Sept 2013, d low dose diphtheria

Diphtheria, tetanus, pertussis (whooping cough), polio and Hib are combined into one injection - the DTaP/IPV(polio)/Hib vaccine.

Five doses of the combined diphtheria, tetanus and polio vaccine are enough to provide long-term protection through adulthood. Pneumococcal conjugate vaccine (PCV) is a separate injection. Meningitis C vaccine (MenC) is sometimes given as a separate injection but is combined with Hib for one injection. Td/IPV(polio) is tetanus, low-dose diphtheria and polio vaccines combined as one injection.

Adult Immunisation

Influenza (see below)

Pneumococcal (>65 yrs, COPD, diabetes, chronic diseases)

Hepatitis B (health workers, at-risk groups, see below)

Chickenpox (non-immune healthcare workers)

Travel, etc

Pneumonia: BTS update October 2009.

Organisms (commonest):

General	<i>S pneum, H infl,</i>
COPD	<i>Above, plus: Mor catarrhalis</i>
Post influenza	<i>S aureus</i>
Young people, episodic	<i>Mycoplasma</i>
Severe, cavitating	<i>Klebsiella</i>
Atypicals	<i>Clamydophila pneumonia and Cl psittaci</i>
Bronchiectasis and cystic fibrosis	<i>Burkholderia cepacia, P aeruginosa</i>
Legionnaires	<i>L pneumophila</i>

Sputum – useful if no antbtcs yet, or severe and failed 1st line. In severe/failed & no sputum consider lower resp tract samples (eg bronchoscopy washings) .

Blood cultures – for moderate and severe.

Urine antigens - severe pneumonia, for *S pneum*, and legionella.

Mycoplasma – epidemics every few years, younger patients, becoming rarer. Diagnosed on PCR or serology

Legionella, water sources, 2-10 days incbtn, can be severe-renal failure & septic shock, 30% GI features, relative bradycardia, 30% imported.

Cavitation - Klebsiella, *S aureus*

Antibiotics (BTS 2009)

Discharge: Amoxicillin (alternatives doxycycline and clarithromycin)

Admitted, mild-mod: –amoxclln plus erythromycin or clarithromycin (alternatives inc moxifloxacin, levofloxacin, doxycycline).

Severe: co-amoclv + macrolide.

CURB-65

5-point score, one point for each of Confusion, Urea >7 mmol/l, Respiratory rate 30/min or more, systolic Blood pressure below 90mmHg (or diastolic below 60mmHg), Age 65 years or older.

0-1, low risk of death and do not normally require admission (<3% mortality)

2 increased risk of death, admission should be considered (9% mort)

3 or more are at high risk of death and require admission (15-40% mort)

Consider social factors also.

Influenza

Types A, B, C. A is most severe. Circulate among birds and pigs – act as reservoirs, 15 H (haemagglutinin) and 9 N (neuraminidase) subtypes. Antigenic drift over time, major sudden antigenic change known as shift. Treatments: Oseltamivir (oral) and Zanamivir (inhaled, iv), shorten by 1/7, not clear if reduce complications.

Animal to human transmission initially. Pandemic if human-to-human transmission

- Swine flu H1N1 (20% infected, 0.02% mortality, 18,000 died)
- Bird flu H5N1 (2003, 628 cases, 60% mortality)
- Bird flu H7N9 (2013 125 cases to 2nd May, 20% mortality)

Vaccination (inactivated, 70% effective, reduce complications in elderly); given to elderly, chronic

disease, pregnancy, health workers. (2012/13 serotypes of H3N2, H1N1, Inflz B)

Middle-East Respiratory Syndrome Coronavirus (MERS-CoV)

130 cases since 2012, 40% mortality. Novel coronavirus, middle-east. Low person-person spread. Possibly zoonosis (?bats). Causes severe respiratory illness with consolidation, associated renal failure is common.

Meningitis

UK annual cases

All meningococcal meningitis & septicia	Mening Gp B only	Pneumococcal mening	Haemophilus influen mening	TB Meningitis	Other Cases
1469	1309	407	33	202	392

Immunocompetent

Organisms: Viral (enterovirus and others), bacterial

Meningococcal early signs: leg pain, cold hands and feet, altered colour.

Meningococcal septicaemic >50% mortality, whereas meningitis about 10% mort.

Pneumococcal meningitis has highest mortality, 20%

Antibiotics: Blind: cefotaxime or ceftriaxone. Chloramphenicol for severe penicillin allergy.

Prophylaxis

rifampicin or ciprofloxacin

Immunisation – Men C, based on polysaccharide coat. One dose in adults/ older children.

Vaccine for types A,C,W and Y also available for travellers, especially pilgrims to Saudi Arabia.

Immunocompromised

- Listeria (amoxicillin iv), esp for travellers to
- Cryptococcal (amphotericin, fluconazole)

Hepatitis

Hepatitis A

- Faeco-oral transmission
- Most UK cases imported
- No chronic carrier state
- 4/52 incubation, brief prodrome, <1% mortality. Full recovery.
- Vaccination inactivated virus, 2nd dose 6/12 then 95% effective for two years.
- Passive immunisation can be given (pooled from blood donors) but less useful

Hepatitis B

- Parenteral and vertical transmission
- Incubation average 60-90 days, Prodromal illness
- Fulminant hepatic failure rarely
- Chronic carrier state – may be stopped by antiviral therapy including interferon.
- Chronic hepatitis may lead to cirrhosis and hepatocellular carcinoma.

- Immunisation – recombinant DNA. Three doses. 10% non-responders.
- Passive immunisation exposed neonates, needlesticks, sexual

Hepatitis serology

- Hepatitis B surface antibody (anti-HBs): previous infection, vaccination, no longer infectious
- Hepatitis B surface antigen (HBsAg): earliest marker of infection, in absence of e-antigen may indicate carrier state
- Hepatitis B e-antigen (HBeAg): marker of infectivity, and (disappearance) marker of recovery
- Anti-hepatitis B core antibody (anti-HBc): persists for life in both carriers and those who have cleared the infection.

Hepatitis C

- Blood transfusion (UK before 1991), IV drug abusers. 3% risk from needle-stick from infected patient.
- Acute infection usually asymptomatic
- 80% become chronic carriers. 0.5% UK, 3% worldwide.
- Diagnosis by ELISA. PCR to prove chronic carrier state.
- 95% eventually have cirrhosis (30% in 20 years).
- Antivirals, inc interferon are very effective.

Gastroenteritis

Toxin related

- Staph, B cereus, C perfringens
- C difficile (Gm+ bacillus, 3% healthy & 20% hospital population, spore forming – survive months, diagnosis from stool toxin, causes pseudo membranous colitis, associated cephalosporins and others, treated with metronidazole or vancomycin, 25% mortality in most susceptible, alcohol gel ineffective)

Small bowel diarrhoea

- Campylobacter (undercooked chicken, contact with animals, children and elderly, bloody diarrhoea, erythromycin if very early, can trigger Guillain-Barré syndrome)
- Salmonella (declining in UK, chicken, many serotypes, some more aggressive, haematogenous spread in imported typhoid and paratyphoid and sometimes in UK strains causing endocarditis, abscesses etc.)
- E coli (travellers' diarrhoea)
- Verotoxic E coli 0157 (related to haemolytic uraemic synd, haemorrhagic colitis)
- Giardia lamblia (protozoan, acute and chronic, stool examination, metronidazole)
- Yersinia enterocolitica (Gm - bacillus, young people, terminal ileitis)
- Reactive arthritis (Reiter's syndrome) linked to campylobacter, shigella and salmonella (also to gonorrhoea and Chlamydia)

Large gut pathogens:

- Shigella (declining in UK, 4 types, usually imported, also care homes, bloody diarrhoea)

- Entamoeba histolytica
- Verotoxic E coli 0157. Usually from cows' intestines, so in meat, or manure contaminated food – bean sprouts. Cause 90% of haemolytic uraemic syndrome

Viral

- Rotavirus *Commonest in infants – nearly all by age 5*
Illness can be severe, dehydration etc, many admissions

Lasts 3-8 days. Lasting immunity
- Norovirus. (small round structured virus, winter vomiting virus, Norwalk-like virus)
Commonest cause infectious gastroenteritis, Immunity is not long-lasting (weeks only), Common in institutions, hospitals etc

UTIs

Organisms

- E coli
- Klebsiella
- Proteus

Dipsticks

- Nitrite only produced by bacterial cleavage of nitrate, so high specificity, but low sensitivity.
- Leukocyte esterase, produced by neutrophils. False +ve from vaginal discharge, higher sensitivity than nitrite, but lower specificity.

Antibiotics

- trimethoprim, nitrofurantoin, local resistance patterns

In Children

- association with ureteric reflux, risk of chronic renal failure from kidney scarring

STDs

N gonorrhoea (ceftriaxone, cefixime or spectinomycin)

Chlamydia trachomatis (doxycycline)

Syphilis (T pallidum) primary, secondary and tertiary (depot penicillin)

Reagin tests

- RPR, VDRL
- False positives in other infections, pregnancy
- Track course of treatment

Treponemal tests

- T. pallidum haemagglutination assay (TPHA)
- T. pallidum particle agglutination test (TPPA)
- fluorescent treponemal antibody absorption test (FTA-abs)
- High specificity
- Permanently positive

Genital herpes (HSV 2, primary may be very painful, relapses (average 4/yr)),

Papillomavirus (16 and 18 related to cervical cancer)

Trichomonas vaginalis

Pubic lice

Gut-related infections

Cholecystitis, diverticulitis, appendicitis etc

Gram negatives

- E coli, Proteus, Klebsiella, Enterobacter, etc

Anaerobes

- Bacteroides

Septic shock

- sepsis bundles etc. <http://www.survivingsepsis.org>. Activated protein C in severe cases

Chickenpox

Viral prodrome

Crops of spots at different stages

Infectious until last spots appear

Complications

Secondary infection

Viral pneumonia

Encephalitis

Acyclovir for infection in risk groups

Immunoglobulin for exposure in late pregnancy

Measles

Viral prodrome

Koplik's spots

Rash from 3rd day, starts face

Infectious for 4 days of rash

Complications common

Otitis media, diarrhoea, pneumonia, immune suppression, encephalitis

Prevention - MMR

Mumps

Headache and fever

3rd day parotid pain and swelling (one or both) +/- oedema

Complications

Oophoritis, orchitis, aseptic meningitis, deafness

30% subclinical

Infectious for several days after parotid swelling (low infectivity)

Rubella

Coryzal prodrome

Rash, pink macules which coalesce. Behind ears to face, then trunk, then extremities

Nodes, sub-occipital, post-auricular

Arthralgia in older patients

Confirmation: IgM, IgG, PCR etc

Vaccination, congenital rubella

Whooping cough

Starts with cough, whoop begins after 2-3 weeks (not in young infants)

Lasts 2-3 months ('100 day cough')

Associated vomiting

Young infants most severe (50% admission)

Treatable early stages with macrolides

Increasingly recognised in adults

Roseola Infantum

Caused by Human Herpes Virus 6 (HHV-6)

3-4 days fever

Rash appears as fever settles

Small number discrete pink spots

Erythema Infectiosum (Fifth disease, slapped cheek syndrome)

Caused by parvovirus B19

Coryzal prodrome

Erythema of cheeks, spreading down

Occasional arthralgia

Risk of aplastic crises in sickle disease

5% risk fetal death or hydrops in pregnancy

Skin and soft tissue infections

Common organisms

- *S pyogenes* erysipelas, cellulitis
- *S aureus* pustules, abscesses, impetigo, scalded skin syndrome. Panton-Valentin Leukocidin (PVL) toxic substance produced by some strains, rare in UK.
-

Gram negatives 'below the waist'

Anaerobic infections

- Tetanus (incubation 7-10 days, local inflammation, exotoxin tetanospasmin, spasms and rigidity, also autonomic features – sweating, tachycardia, raised BP. recovery by regrowth of axonal terminals). Vaccination toxoid, . Passive immunisation.
- Gas-gangrene (*C perfringens*, rapid toxin mediated tissue destruction, gas producing)
- Necrotising fasciitis (Fournier's gangrene in scrotum/groin area, mixed infection aerobes and anaerobes, debridement)

Herpes viruses

- Herpes simplex
 - Type 1. 90% by 2 years. Recurrent 'cold sores'
 - Type 2. Genital. Painful reactivations.
- Herpes zoster
 - Chicken pox. Shingles.
- EBV
 - Infectious mononucleosis. (incubation 5-7 weeks, young people, sore throat, lymphadenopathy, rare hepatosplenomegaly and splenic rupture. Atypical lymphocytes, Paul Burnell and Monospot tests – false positives in RA, Hep A, CMV and lymphoproliferative disorders.
- CMV
 - 70% adults have had CMV. Usually asymptomatic or mild. Illness in utero and immunocompromised. May affect any organ.

Zoonoses

Approx UK reported cases in 2012 (lab reports, some acquired abroad)

Anthrax	4
Toxoplasmosis	300
Leptospirosis	70
Lyme Disease	900

Toxoplasmosis. Protozoan. Pathogen of cats. Infection in most people, but asymptomatic. May affect eyes. Causes intra-uterine infection. Reactivation in immunocompromised, encephalitis.

Leptospirosis (Weil's Disease). Rat urine, water, sewers. Crosses broken skin. Fever, jaundice, later renal failure. Penicillin

Lyme Disease. Borrelia burgdorferi, hard ticks, reservoir in deer. Early localised disease (erythema chronicum migrans). Late disseminated disease (months). Polyneuropathy, AV block, arthritis. Doxycycline.

Scabies

Hands, axillae, wrist and genitals, face in babies, symptoms after six weeks. In immunocompromised may develop massive infection: Norwegian scabies
Treatment Permethrin.

Bone and joint infection

Osteomyelitis and septic arthritis

- S aureus, strep, gram negatives
- Salmonella in sickle cell disease
- TB

Tends to affect more vascular bone, proximal tibia, distal femur, proximal humerus

Sequestrum, involucrum

PVL positive staphylococci

(Panton-Valentine leukocidin) rare cause of skin infections which are more aggressive and necrotising than other staphylococci.

HIV and AIDS

80,000 in UK, 25% undiagnosed.

Seroconversion illness 1-6 weeks, affects up to half. Glandular fever like.

Targets CD4 (helper cells)

Total T lymphocytes constant as CD8 (killer) cells increase. CD4 <200=AIDS, <350 advised

combination anti-retrovirals.

Opportunistic infections

Needlestick policies, 3/1000 risk from percutaneous exposure, 1/1000 mucocutaneous exposure. PEP 80% effective, ideally < 1 hr, but must be <2-3/7. 50% side effects, 30% discontinue – aim is 4/52 therapy. Can be used in pregnancy.

Infective endocarditis (IE)

Viridans streptococci (45-50%), Indolent course; mostly affects abnormal valves.

Infections usually are penicillin sensitive.

Staphylococci (25%) Affects normal valves.

A big problem in IV drug abusers, causes acute fulminant endocarditis.

S. epidermidis common in patients with indwelling catheters.

Associated with a high rate of metastatic embolisation.

Enterococci (10%).

Inhabit gastrointestinal and genitourinary tracts.

Following GI or GU instrumentation.

Less common organisms causing IE include:

Gram-negative organisms such as H.influenzae, N.gonorrhoea and pseudomonas species.

- Brucella and chlamydia.

- Rickettsial infection (e.g. Coxiella Burnetti causing Q fever)

- Fungi especially in immunosuppressed patients and in prosthetic valves.

Bacteriocidal or bacteriostatic?

Bacteriocidal:

Penicillin, cephalosporins, aminoglycosides, fluoroquinolones, nitrofurans, vancomycin, monobactams, co-trimoxazole, and metronidazole.

Bacteriostatic

Tetracyclines, sulphonamides, spectinomycin, trimethoprim, chloramphenicol, and macrolides.

Malaria

Life cycle

- Sporozoites injected by mosquito infect liver
- Dormant stage in liver – hypnozoites
- From liver merozoites infect RBCs
- Multiplication stage in RBCs – schizonts
- Gametocytes, produced later, are infective to mosquitos

falciparum

- Predominantly Africa, tropics and sub-tropics
- infects young red cells
- May have high parasitaemia
- Complications related to schizogeny
- No dormant stage
- Treatment: quinine, (iv > 2%), plus tetracycline (other options)

Vivax and ovale

- Ovale: W Africa, Vivax where malaria endemic outside Africa (inc temperate regions)

- Have dormant, hypnozoite phase (risk of relapse)
- Alternate day fever
- Treat chloroquine, primaquine to prevent relapse

Malariae

- Rarest
- Longest incubation (can be months or years)
- No dormant phase
- Associated nephrotic syndrome
- Treat chloroquine

Incubation periods

Gastroenteritis

Hours (toxins)

S aureus exotoxin 1-10 hours (cream, macaroni)

B cereus 1-6 hours (fried rice kept warm)

S perfringens 12-24 hours (reheated meat)

Days

Salmonella 2-3 days

Campylobacter 2-5 days

Other bacterial condition

Diphtheria: 2-9 days

Tetanus: 1 day - 2 months (commonly 7-8 days)

Pertussis (whooping cough): 5-21 days (commonly 7 days, rarely more than 10)

Viruses

Measles: 6-21 days (commonly 10 days)

Chickenpox: 10-21 days

Fifth disease ('slapped cheek' syndrome): 13-18 days

Mumps: 16 to 21 days

Rubella (German measles): 14 to 21 days

Glandular fever 4-6 weeks

Hepatitis A 15 to 45 days (average 30)

Hepatitis B 1 to 6 months

Malaria

P falciparum malaria 8 days to months (usually short)

P vivax and P ovale 14 days to months

P malariae 3 weeks to months (may be long)

Infective endocarditis

The causative organism is usually a bacterium but other organisms may be involved and therefore IE is a better term to use rather than the traditional terminology "bacterial endocarditis".

The commonest organisms involved in non-intravenous drug abusers are streptococci (45-50%), staphylococci (25%) and enterococci (10%).

- Streptococci: Most of the viridans type (β -haemolytic type).
Commensals of the oropharynx.

Cause IE following dental procedures or bronchoscopy.
 Indolent course; mostly affects abnormal valves.
 Infections usually are penicillin sensitive.

- Staphylococci: Affects normal valves.
 A big problem in IV drug abusers.
 S. aureus causes acute fulminant endocarditis.
 Intravascular catheters pose a potential risk.
 S. epidermidis common in patients with indwelling catheters.
 Associated with a high rate of metastatic embolisation.
 Can be multi-drug resistant (e.g. MRSA).
- Enterococci: Inhabit gastrointestinal and genitourinary tracts.
 Following GI or GU instrumentation.
 Growing incidence of antibiotic resistance (e.g. VRE).

Less common organisms causing IE include:

- Gram-negative organisms such as H.influenzae, N.gonorrhoea and pseudomonas species.
- Brucella and chlamydia.
- Rickettsial infection (e.g. Coxiella Burnetti causing Q fever)
- Fungi especially in immunosuppressed patients and in prosthetic valves.

Antibiotics

Antibiotic	Susceptible bacteria	Notes
Penicillin V	S viridans (some resistance), S pyogenes (all)	Cell wall disruption. Modest oral absorption as acid-labile. (bioavailability of oral dose 60%).
Penicillin G	Same spectrum as Pen V	Given parenterally
Amoxycillin	Extended spectrum compared to Pen, including some Gm –ves, but some resistance in S pneum and H infl.	Oral bioavailability 95%. Some allergic reactions. Rash in infect mononucleosis.
Co-amoxiclav	Beta-lactamase inhibited by clavulanic acid. Broad Gm +ve and Gm –ve spectrum.	Tazocin Piperacillin/tazobactam is similar with an even greater spectrum, parenteral only.
Extended spectrum penicillins	Extended spectrum Gm +ve and Gm –ve and some anaerobes	Examples piperacillin, azlocillin, ticarcillin. Parenteral therapy. Synergy with aminoglycosides.
Cephalosporins	Four generations, increasing gm –ve effectiveness, some loss Gm +ve effectiveness. Some third generation are anti-pseudomonal. Third generation used for gonorrhea.	Cell wall disruption. Less penicillinase susceptible than Pen V. For penicillin allergy, sensitivity likely to first generation in 10%, but not to later generation ceph. Popularity declined as associated C diff, and many alternatives.
Sulphonamides	Some Strep, Staph, E coli	Anti-folate. Allergic reaction in 3% (60% HIV)

	and H infl.	patients). Now not in regular use other than as part of co-trimoxazole.
Trimethoprim	UTIs particularly E coli, resistance patterns vary. With sulphonamide for pneumocystis.	Anti-folate. Well absorbed orally.
Macrolides	Erythromycin – similar to Penicillin. Also mycoplasma, and atypical pneumonias. Camp jejuni, B pertussis. Clarithromycin – similar to erythromycin but greater Gm +ve activity	Bind to ribosomes and inhibit protein synthesis. GI side-effects limit dosing, more marked with erythromycin. Clarithromycin is more acid stable so greater oral bioavailability. Inhibit cytochrome P450 so increase levels of many other drugs (eg simvastatin). This effect is worse with erythrmec. Clarithromycin has good tissue penetration so can be used for soft-tissue infections. Prolong QTc, associated arrhythmias.
Clindamycin	Anaerobes, Gm +ves,	Bind to ribosomes and inhibit protein synthesis. 90% oral bioavailability. Good tissue penetration so useful for osteomyelitis. Effective for many MRSA isolates. Strongly associated with C diff.
Tetracyclines	Malaria, rickettsia, Chlamydia, Lyme disease	Bind to ribosomes and inhibit protein synthesis. Doxycycline is main agent, as better absorbed, and daily dosing. Teratogenic (teeth and bones). Photosensitising. Can cause raised CSF pressure.
Aminoglycosides (eg gentamicin)	Gm –ves. Majority are susceptible, but some resistance, some plasmid mediated. S aureus.	Protein synthesis inhibition. Not absorbed orally. Synergistic with penicillin. Highly effective. Toxicity ears and kidneys, therapeutic monitoring
Glycopeptides (vancomycin and teicoplanin)	Gm +ves, C diff	Disrupts cell wall synthesis. Not absorbed orally, so useful orally for C diff. Main use for MRSA.
Nitrofurans	Gm –ves. Good for E coli, no activity Proteus or Pseudomonas.	Damages bacterial DNA. 25% of oral dose concentrated in urine. Poor tissue levels, so not for pyelonephritis. Antagonises quinolones Hypersensitivity reactions, including pulmonary fibrosis.
Quinolones	Broad-spectrum, especially Gm –ve. Newer agents like moxifloxacin and levofloxacin active against strep	Disrupt DNA. Most important cause of MRSA and C diff internationally. Widely misused. Cause tendon rupture. Good oral absorption and tissue penetration. Reduced by antacids
Metronidazole	Anaerobes and protozoa, also C diff, H pylorii	Well absorbed orally. Well tolerated. Alcohol reaction. peripheral neuropathy

Chloramphenicol	Broad-spectrum	Disrupts protein synthesis. Causes aplastic anaemia, so no longer first-line except as eye drops. Penetrates brain very well. Well absorbed orally.
Fusidic acid		Disrupts protein synthesis. Good antistaphylococcal activity, but resistance develops rapidly. Avoided if combined with another drug.

Bacteriocidal or bacteriostatic?

Bacteriocidal antibiotics kill bacteria; bacteriostatic antibiotics only slow their growth or reproduction.

Penicillin is a bactericide, as are cephalosporins. Aminoglycosidic antibiotics can act in both a bactericidal manner (by disrupting cell wall precursor leading to lysis) or bacteriostatic manner (by binding to 30s ribosomal subunit and reducing translation fidelity leading to inaccurate protein synthesis)

Other bactericidal antibiotics include the fluoroquinolones, nitrofurans, vancomycin, monobactams, co-trimoxazole, and metronidazole.

Bacteriostatic antibiotics hamper the growth of bacteria by interfering with

1. bacteria protein production,
2. bacteria DNA production,
3. bacteria cellular metabolism.

Bacteriostatic antibiotics inhibit growth and reproduction of bacteria without killing them; killing is done by bactericidal agents.

Bacteriostatic agents must work with the immune system to remove the microorganisms from the body. High concentrations of most bacteriostatic agents are also bactericidal, whereas low concentrations of bacteriocidal agents are only bacteriostatic.

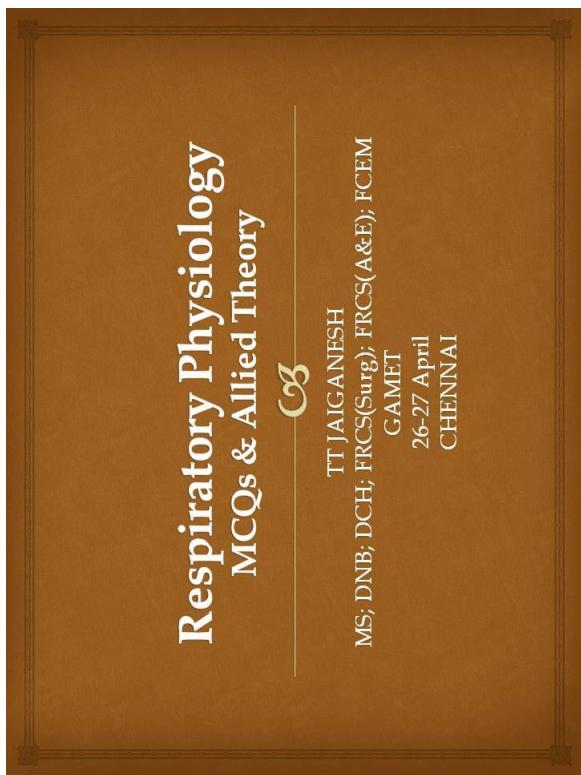
This group includes the tetracyclines, sulphonamides, spectinomycin, trimethoprim, chloramphenicol, macrolides and lincosamides.

Notifiable Diseases in UK

Acute encephalitis	Plague
Acute poliomyelitis	Rabies
Anthrax	Relapsing fever
Cholera	Rubella
Diphtheria	Scarlet fever
Dysentery	Smallpox
Food poisoning	Tetanus
Leptospirosis	Tuberculosis
Malaria	Typhoid fever
Measles	Typhus fever
Meningitis	Viral haemorrhagic fever
meningococcal	
pneumococcal	
haemophilus influenzae	
viral	
other specified	
unspecified	

Meningococcal septicaemia (without meningitis)	Viral hepatitis Hepatitis A Hepatitis B Hepatitis C other
Mumps	Whooping cough
Ophthalmia neonatorum	Yellow fever
Paratyphoid fever	

I Stell



Regarding the control of respiration

- ☞ a. neurons generating the spontaneous rhythmicity of breathing are located in the medulla (T)
- ☞ b. stretch receptors in the lung form spinal reflexes to control depth of breathing (F)
- ☞ c. central chemoreceptors increase respiration in response to falling oxygen (ppO_2) in the cerebral circulation (F)
- ☞ d. oxygen receptors become largely inactive in patients with COPD and chronic CO_2 retention (F)



Control of Respiration: 2

- ☞ Respiration is influenced by PaCO_2 , arterial pH and hypoxia
- ☞ PaCO_2 acts on central chemoreceptors
- ☞ PaO_2 acts on peripheral chemoreceptors
- ☞ pH acts on both
- ☞ Central chemos: floor 4th Ventricle, responds to changes in csf pH
- ☞ Peripheral chemos: carotid and aortic bodies respond to hypoxia, pH and blood flow

Control of Respiration: 1

- Respiration is regulated by respiratory neurones (floor of fourth ventricle)
- Arterial CO_2 is tightly regulated around 5.3 kPa (40 mmHg)
- Main determinant of VE is CO_2 production (VCO_2)
- VCO_2 determined by metabolic rate and energy substrate
- Respiration modified by other factors:
 - Higher centres (including cortex), speech, eating & drinking, anticipation of exercise, exercise itself

Concerning lung volumes and capacities

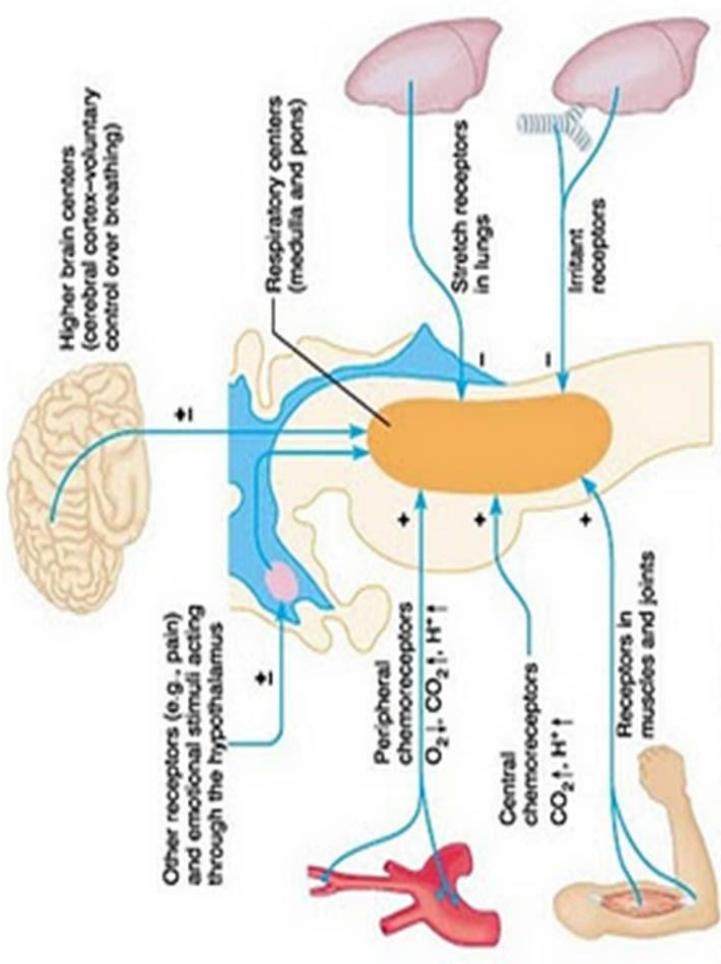
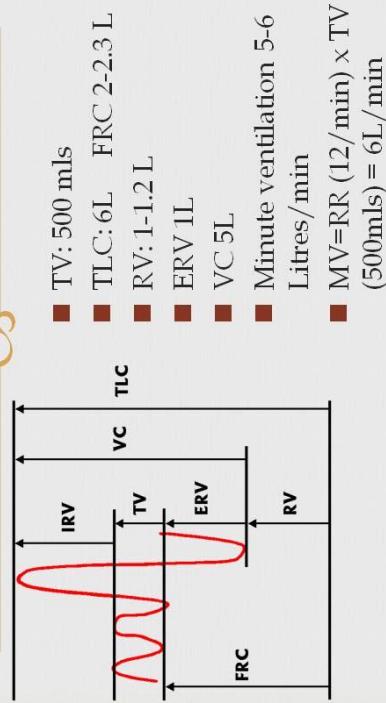
Q a. a healthy male has a tidal volume of around 500ml
(T)

Q b. the vital capacity is reduced in asthmatics
(F)

Q c. patients with restrictive lung disease typically have an FEV₁/FVC ratio >80%
(T)

Q d. total lung capacity (TLC) may be calculated by helium dilution but not by spirometry
(T)

- Some ball-park figures



Lung volumes & their measurement:

- Lung volumes (Spirometry): FEV₁ and FVC (FEV₁/FVC>75%: normal (with FEV₁ and FVC within normal ranges))

- VC + RV = TLC
- FRC + IC = TLC
- FRC + IC = RV + VC
- FRC = ERV + RV

Lung volumes & their measurement: 2



❑ OBSTRUCTIVE LUNG DISEASE: COPD (emphysema)

❑ FEV₁/FVC <75%

❑ Raised TLC, RV, RV/TLC ratio (normal is 20%) and FRC

❑ Reduced KCO

Lung volumes & their measurement: 3



❑ RESTRICTIVE LUNG DISEASE

❑ FEV₁/FVC >75%: (with reduced FEV₁ and FVC values)

❑ Reduced TLC, RV, FRC, VC, FEV₁

❑ Reduced KCO : interstitial lung disease

❑ Raised KCO: Respiratory muscle weakness

Posture



- ❑ Lying supine small drops in TLC and VC
- ❑ Largest change is fall in FRC
- ❑ Postural drop of VC (normally 200 mls and decreases with age)
 - ❑ Very important in evaluating diaphragmatic function
 - ❑ >20% drop from sitting to supine VC signals significant diaphragm weakness

Regarding the measurement of peak expiratory flow rates (PEFR)

- ❑ a. PEFR is independent of lung volume (F)
- ❑ b. expected readings for an adult woman would be 300-350 L/min (F)
- ❑ c. is useful in determining the reversible component of disease in chronic obstructive pulmonary disease (COPD) (T)
- ❑ d. readings below 33% of normal or expected indicate mild to moderate asthma (F)

The functional residual capacity (FRC)

- ❑ a. is measured by spirometry (F)
- ❑ b. is the volume of air in the lungs when there is no respiratory effort (T)
- ❑ c. corresponds to the volume at 50% of the inspiratory flow-volume curve (F)
- ❑ d. does not contribute to total lung capacity (TLC) (F)

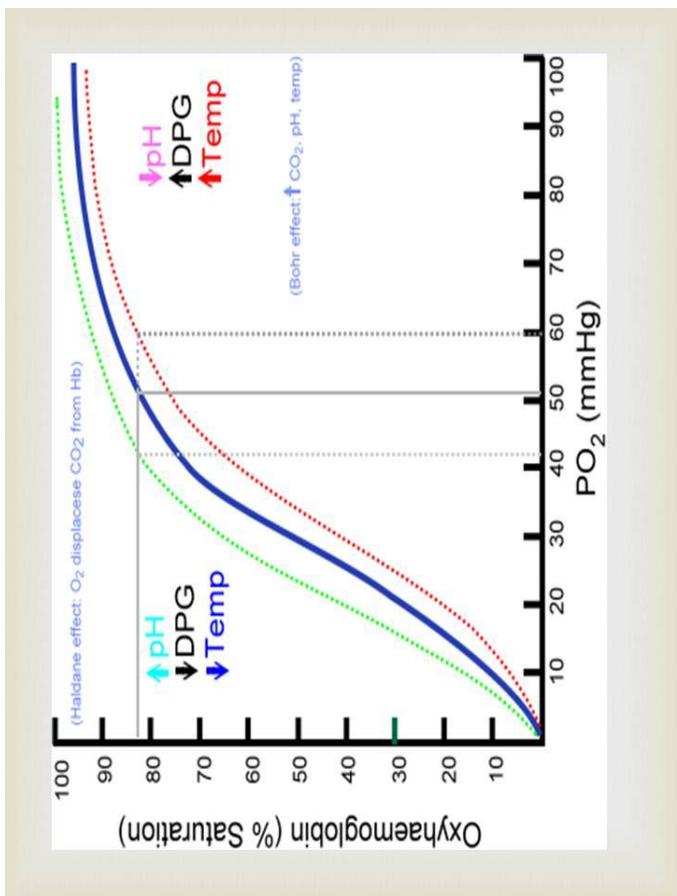
Regarding alveolar anatomy

- ❑ a. goblet cells secrete surfactant (F)
- ❑ b. type I alveolar pneumocytes comprise the majority of alveolar surface area (T)
- ❑ c. smooth muscle fibres in the alveolar walls facilitate passive expiration (F)
- ❑ d. prostaglandins increase surfactant production in premature babies (F)

- Surfactant is a complex substance containing phospholipids and a number of apoproteins (T)
- Produced by the Type II alveolar cells, and lines the alveoli and smallest bronchioles (F)
- Reduces surface tension throughout the lung, thereby contributing to its general compliance (T)
- It is also important because it stabilizes the alveoli

Regarding the binding of oxygen to haemoglobin in arterial blood

- ❑ a. left shift of the haemoglobin-oxygen dissociation curve means more oxygen binds to haemoglobin for a given partial pressure of oxygen (PaO_2) (T)
- ❑ b. 2,3-diphosphoglycerate (2,3-DPG) increases the affinity of haemoglobin for oxygen (F)
- ❑ c. acidosis shifts the haemoglobin-oxygen dissociation curve to the right (T)
- ❑ d. methaemoglobin shifts the haemoglobin-oxygen dissociation curve to the left (T)



Regarding the binding of oxygen to haemoglobin in arterial blood

- ❑ a. acidosis raises oxygen saturation for a given PaO₂ (F)
- ❑ b. 2,3-diphosphoglycerate (2,3-DPG) increases the affinity of haemoglobin for oxygen (F)
- ❑ c. hypothermia shifts the haemoglobin-oxygen dissociation curve to the left (T)
- ❑ d. exhibits positive cooperativity (T)

Oxy-Hb dissociation curve

- ❑ 2 anchor points:
- ❑ 100 mmHg = 97% SpO₂
- ❑ 40 mmHg = 75% SpO₂
- ❑ Flat after 60 mmHg : 80% SpO₂
- ❑ Left shift in lungs : aim to take up O₂ to tissues (foetal Hb)
- ❑ Right shift in muscles: aim to give up O₂ to tissues
- ❑ Right shift: Increasing temp, CO₂, low pH (Bohr effect), increasing 2,3 DPG (increased in hypoxia)

The following are true of pulse oximetry

- ❑ a. bilirubinaemia gives a falsely high saturation (F)
- ❑ b. carboxyhaemoglobin gives falsely low readings (F)
- ❑ c. readings of 90% roughly correspond to a pO₂ of 8.0 kPa as measured by arterial blood gas analysis (T)
- ❑ d. peripheral vasodilatation due to CO₂ retention causes unreliable readings (F)

Pulse oximetry: 1

- ☞ Detects light transmitted at 2 wavelengths corresponding to deoxygenated and oxygenated HB
- ☞ Light emitters and detectors face each other separated by finger/earlobe
- ☞ Signal is the difference in absorbance between peripheral systolic pulse wave and subsequent diastole

Pulse oximetry Problems : 2

- ☞ Carboxy and Meth HB cannot be distinguished from OxyHB so SpO₂ overestimation in Meth or Carboxy HB
- ☞ Response time is slow; instrument delay (10-15 secs) and circulatory delay; exaggerated by vasoconstriction and low cardiac output
- ☞ Gives no idea of ventilation

The following are true of non-invasive ventilation in adults

- ☞ a. improves cardiac output in patients with acute left ventricular failure (T)
- ☞ b. reduces intra-thoracic pressure by reducing the work of breathing (F)
- ☞ c. increases tidal volume (T)
- ☞ d. has no effect on gas exchange (F)

Regarding arterial blood gases

- ☞ a. the liver is the main organ responsible for compensatory changes in response to a respiratory acidosis (F)
- ☞ b. metabolic acidosis is associated with hyperkalaemia (T)
- ☞ c. hyperventilation is the only cause of a respiratory alkalosis (T)
- ☞ d. mixed venous blood has an oxygen tension of 8Kpa (F)

In un-acclimatised persons ascending to high altitudes

- ☞ a. respiratory acidosis occurs (F)
- ☞ b. the oxy-haemoglobin dissociation curve shifts to the left (T)
- ☞ c. pulmonary oedema may occur (T)
- ☞ d. an increase in haematocrit may be seen after 24 hours (F)

Effect of altitude: 1



- ☞ Note partial pressure (barometric pressure) decreases with ascending altitude not composition of air
- ☞ 3000m above sea level alveolar PO₂ is 60 mmHg: hypoxic stimulation...increases ventilation...lowers CO₂...respiratory alkalosis

- ☞ Unacclimatized on air:
- ☞ Symptoms of AMS typically develop within 4-12 hours of arrival at altitude and occur in 40% of individuals ascending from sea level to over 3000 m and in 75% of those ascending to altitudes greater than 4500 m.

Effect of altitude: 2



- ☞ AMS is the presence of headache plus one or more of insomnia, dizziness, lassitude, fatigue, anorexia, nausea or vomiting in an individual who has recently arrived at an altitude of greater than 2500 m.

- ☞ The exact process of AMS remains unknown, however it is known that hypoxia elicits neuro-humoral and haemodynamic responses that result in over perfusion of neurovascular beds, elevated hydrostatic capillary pressure, capillary leakage and consequent oedema in both the brain and the lungs.

Effect of altitude 3: acetazolamide



- Carbonic anhydrase inhibitor
- Increases urinary HCO₃- excretion; counteracts respiratory alkalosis
- Reduces CSF formation; stimulation of nocturnal respiration and reducing nocturnal apnoea ; reducing reduction in blood O₂ saturations
- Reduces incidence & severity of acute mountain sickness (taken before or during ascent)

Effect of altitude: acclimatization

- ☞ Respiratory alkalosis shifts curve to left
- ☞ But increase in 2-3 DPG shifts it to the right
- ☞ The latter is dominant overall: effect is to increase O₂ delivery to tissues
- ☞ Erythropoietin secretion increases promptly
- ☞ This falls somewhat as ventilatory response increases and arterial pO₂ increases
- ☞ The increase in RBCs triggered by EPO begins at 2-3 days and is sustained as long as at high altitude

Regarding the pulmonary circulation

- ☞ a. in the normal lung the ventilation/perfusion ratio steadily decreases from the apex to the base
(T)
- ☞ b. pulmonary blood flow equals cardiac output
(T)
- ☞ c. pneumonectomy maintains a constant ventilation/perfusion ratio
(T)
- ☞ d. mean pulmonary arterial pressure is between 5 and 10mmHg
(F)

Pulmonary circulation: 1

- ☞ Pulmonary vascular bed similar to systemic except walls 30% as thick as aorta & small pulmonary arterial vessels have less smooth muscle v systemic arterioles
- ☞ RV output 5.5L/min at rest (same as LV output)

- ☞ PAP 24/9 : mean pressure 15 mmHg
- ☞ LA pressure during diastole is 8mm Hg so pressure gradient of circa 7 mmHg

Pulmonary circulation: 2

- ☞ Pulmonary capillary pressure is circa 10 mmHg; oncotic pressure is 25 mmHg; gradient of 15 mmHg keeps alveoli dry
- ☞ If Cap pressure > 25 mm Hg: oedema and congestion
- ☞ Mitral stenosis: chronic progressive rise in Cap pressure and fibrotic changes in pulmonary vessels

The following have an effect upon the arterial-alveolar oxygen gradient (A-a gradient)



- ❑ a. acute pulmonary oedema (T)
- ❑ b. increasing age (F)
- ❑ c. hypoventilation (T)
- ❑ d. atrial septal defect (T)

Regarding pulmonary shunts



- ❑ a. they reduce the alveolar -arterial (A-a) gradient (F)
- ❑ b. hypoxia can be corrected by giving 100% oxygen (F)
- ❑ c. alveolar dead space is increased (T)
- ❑ d. pulmonary arteriolar dilatation occurs to compensate (F)

The following are correct when considering gas transfer in alveoli



- ❑ a. occurs primarily through type I pneumocytes (T)
- ❑ b. the partial pressure of alveolar carbon dioxide is roughly 5 kPa (40mmHg) (T)
- ❑ c. carbon dioxide exchange across the alveolar membrane is diffusion limited (F)
- ❑ d. the transfer factor (TLCO) is decreased in asthma (F)

Carriage of O₂



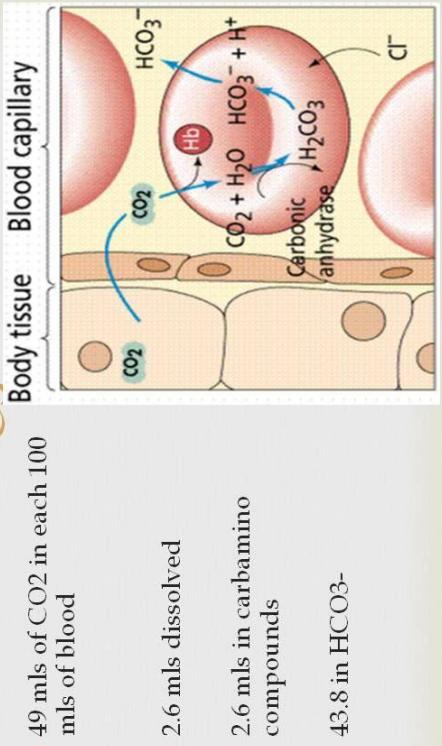
- ❑ O₂ is virtually all carried as combined with Hb (T)
- ❑ Oxygen is poorly soluble in blood (F)
- ❑ HB has 4 molecules of haem: centrally located iron (in ferrous state) to which each oxygen molecule binds (T)
- ❑ Each one makes it easier for the next one to bind...hence sigmoid shape of oxygen dissociation curve (F)
- ❑ 1.34 mls per gram of Hb : normal Hb 15 g/dl so... (T)
- ❑ Each 100 ml of blood contains 20 mls of oxygen (F)

Carriage of Carbon Dioxide: 1



- Solubility of CO₂ 20 times more than O₂
- CO₂ diffuses into RBC and combines with H₂O in presence of carbonic anhydrase to form H₂CO₃
- This dissociates into HCO₃⁻ (enters plasma) and H⁺ (buffered by haemoglobin); chloride shift
- Some CO₂ in RBC's reacts with amino group of proteins to form carbamino compounds
- 11% of CO₂ added to blood in systemic capillaries is carried to lungs as carbamino-CO₂

Carriage of Carbon Dioxide: 2



Lung compliance

- ☞ a. is the measure of the ease of expansion of the lungs
(T)
- ☞ b. is decreased by pulmonary surfactant
(F)
- ☞ c. is increased in chronic obstructive pulmonary disease
(T)
- ☞ d. dynamic compliance may be reduced in asthmatics
(T)

The following increase lung compliance



- ☞ a. emphysema
(T)
- ☞ b. pulmonary oedema
(F)
- ☞ c. severe kyphosis of the spine
(F)
- ☞ d. pulmonary surfactant
(T)

Pulmonary mechanics:



Compliance

ca Expansion of lung and chest wall requires a distending force expressed as volume change per unit distending pressure (mlcm/h20)

Resistance

ca Flow of gas in and out of lungs is opposed by frictional resistance of the airways: (kPas/L)

ca Increased in Emphysema and age (poor recoil pressure)
ca Decreased in pulmonary fibrosis and pulmonary oedema (stiff lungs)

ca Related to lung volume, bronchomotor tone and thickness of mucosal layer
ca Increased in COPD, asthma

Questions?



THANK YOU

**MCEM Part A
PATHOLOGY**

“The candidate needs to have a good understanding of the general pathological processes which present to the Emergency Department or underpin nationally accepted guidelines.”

For the MCEM part A

Mathew Hall BM BCh PhD MCEM
Specialty Doctor Emergency Medicine
Princess Royal University Hospital

The remaining include:

Wound Healing
mechanism
influencing factors
delayed healing

- mechanism
- influencing factors
- delayed healing
- specific tissue responses

Inflammatory Response
acute phase proteins
complement

Immune response
hypersensitivity
immunological marker

Shock
pathophysiology
clinical

Primary -occurs within hours of closure of a full thickness incision

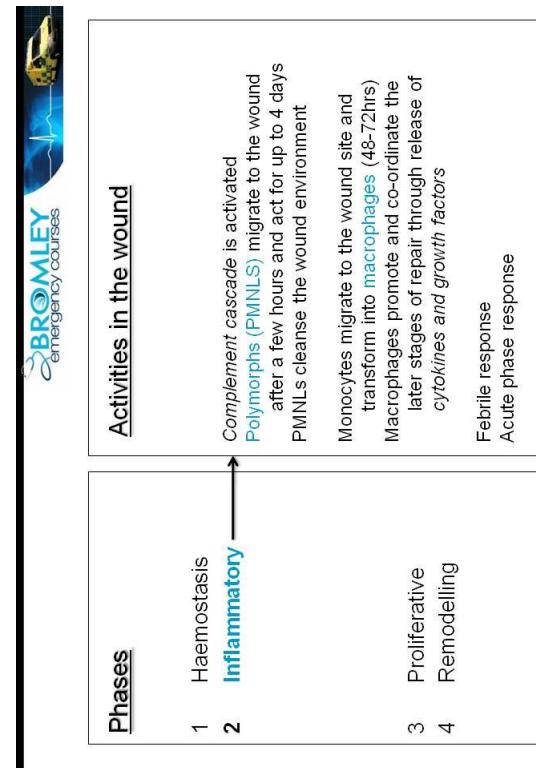
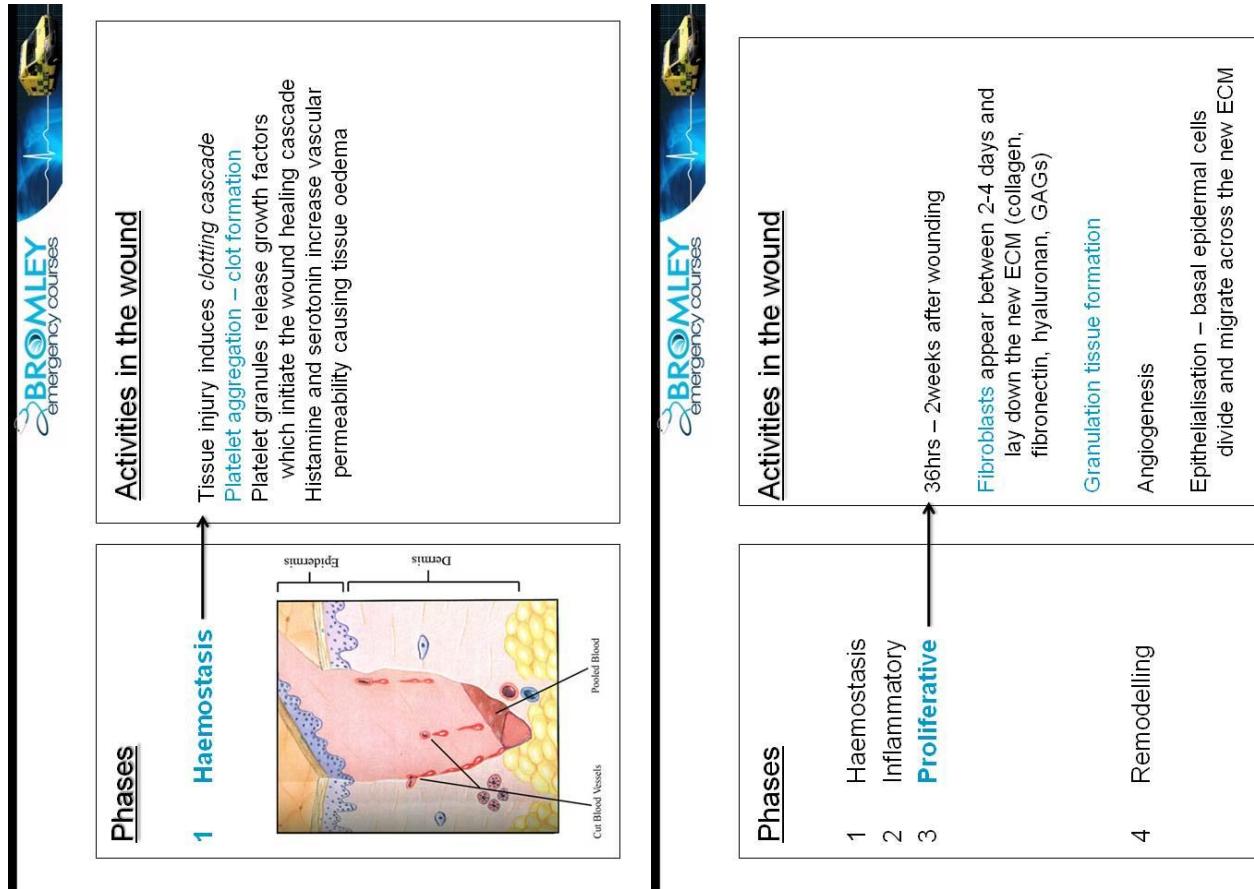
Delayed Primary

- occurs if edges of the wound not immediately approximated
dirty wounds
- may be closed surgically after 4-5 days
- if cleansing incomplete – chronic inflammation and scarring

- unaided closure full t
- pronounced inflammation
- wound contraction in

Phases of wound healing - skin

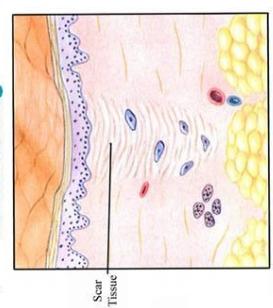
1	Haemostasis
2	Inflammatory
3	Proliferative
4	Remodelling





Phases

- 1 Haemostasis
- 2 Inflammatory
- 3 Proliferative
- 4 **Remodelling**



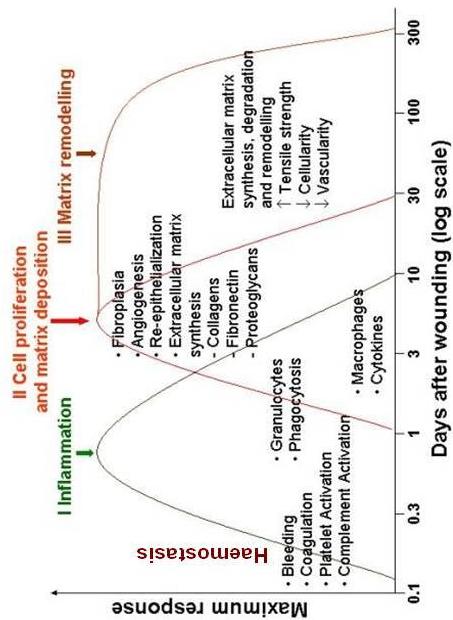
Turnover granulation tissue into ever more organised form (matrix remodelling)

Fibroblasts, macrophages and granulocytes
Myofibroblasts promote wound contraction

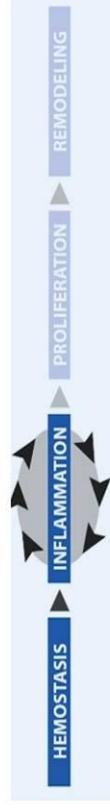
May last up to 300days

Final product is an avascular, acellular scar

Wound Healing Summary

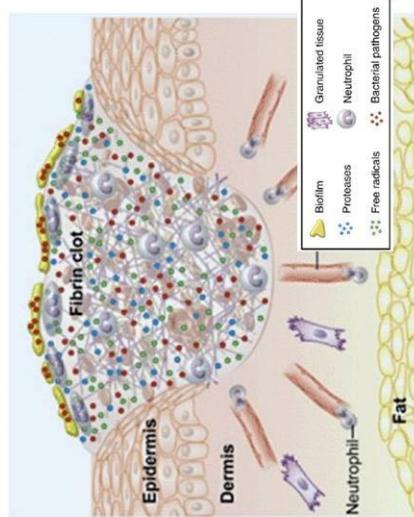


Chronic wounds



Chronic wounds are generated when healing stalls in the inflammatory phase due to:

- infection
- ischaemia/hypoxia/oedema
- underperfusion
- further tissue damage
- cytokine imbalances
- lack of nutrients
- free radical damage



Inflammatory Response

- Inflammation is the complex biological response of vascular tissues to harmful stimuli.
- It is a protective attempt to remove the injurious stimuli + to initiate the healing process.
- Inflammation does not equal infection (Infection is caused by an exogenous pathogen, while inflammation is one of the responses of the organism to the pathogen)
- In the absence of inflammation, wounds and infections would never heal
- Inflammation itself can cause significant injury and requires a mechanism to switch itself off once the injurious stimuli is removed and healing underway
- Chronic inflammation can also lead to a host of diseases





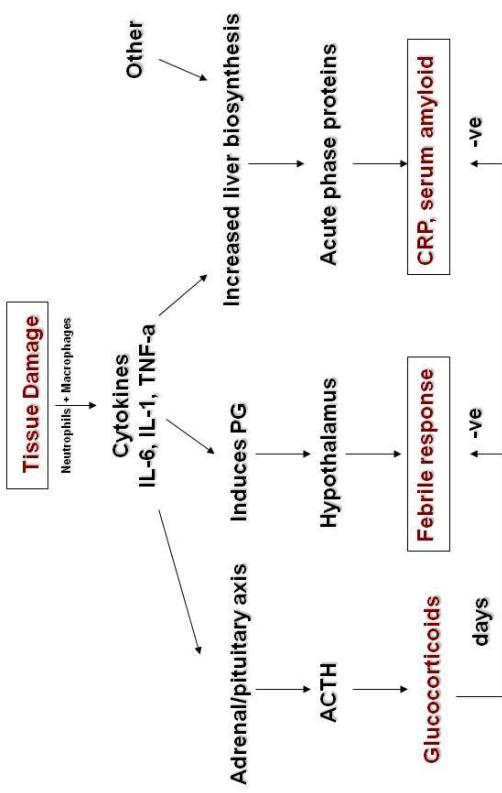
Inflammatory Response

A very complex subject. Four major mechanisms to know about

- Acute phase response
- Complement cascade
- Prostaglandins and eicosanoids
- Kinin - kallikrein system

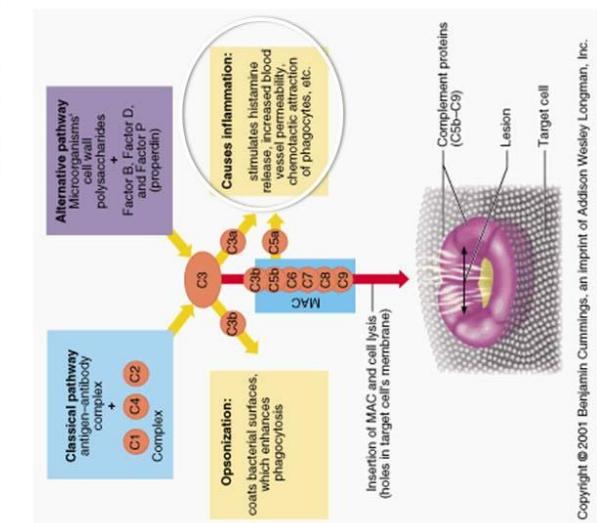
• Also considerable overlap with coagulation pathways, immune system and wound healing

Acute Phase Response

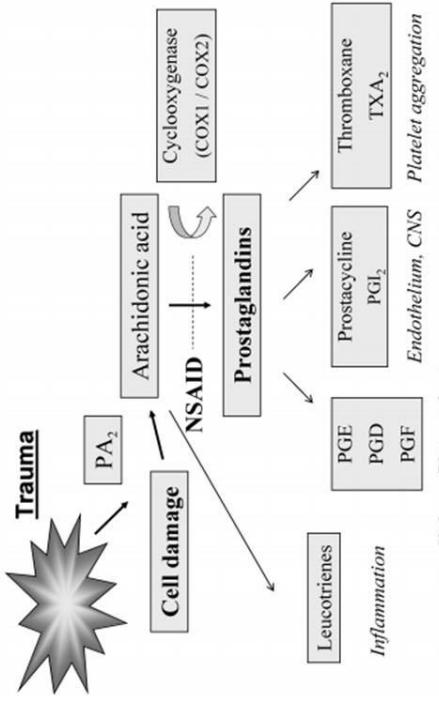


Complement

IgG-antibody complex normally triggers classical pathway of complement activation



Prostaglandin and Eicosanoids



Hypersensitivity

Def.

The abnormal immune response to the presence of a particular antigen

May cause a variety of tissue reactions

4 Types...

Type I

Anaphylactic

Antigen reacts with IgE antibody on sensitised mast cells

Releasing agents which release histamine and vasoactive substances

May be local or systematic
release of all vascular tissue

may be local or systemic

- Atopic diseases
- Drug allergies
- Anaphylactic shock

MG – Ab to Ach receptors

SLE – Ab to antigen in nucleus

Good pastures = Ab to GBM + ayeolar capillaries

The diagram illustrates a mast cell at the top left, with a dashed arrow pointing from its surface to a cluster of small, greyish-blue dots representing inflammatory mediators. The mediators are shown dispersing into a larger area labeled 'tissue' at the bottom right.

Type II

Cytotoxic

Antibody mediated
Circulating antibody (IgM, IgG) reacts with antigen on cell surface
Complement activation and phagocytosis kill cell

eg Transfusion reactions



Type III

Immune complex (IgG/IgM)

Circulating antigen and antibody combine and precipitate out as immune complexes
Immune complexes cause small vessel damage

eg farmers lung
serum sickness



Type IV

Cell mediated (delayed >12hrs)

Antigen stimulate sensitised T-lymphocytes causing release of lymphokines and inflammatory mediators
No Ab response



eg Late graft rejection
Contact dermatitis
Tuberculin skin reaction



Shock

Failure to maintain adequate tissue perfusion : acute failure circulatory function

Classifications

Cardiogenic	e.g. pump failure	Compensated
Hypovolaemic	e.g. haemorrhage	Uncompensated
Distributive	e.g. septic, anaphylactic	Irreversible
Obstructive	e.g. PE, cardiac tamponade	
Dissociative	e.g. profound anaemia	



Hypovolaemic shock

	Class I	Class II	Class III	Class IV
Blood Loss (ml)	Up to 750	750-1500	1500-2000	>2000
% blood loss	Up to 15%	15-30%	30-40%	>40%
Pulse	<100	>100	>120	>140
BP	normal	normal	decreased	decreased +
Pulse pressure	normal or increased	decreased	decreased	decreased
Resp rate	14-20	20-30	30-40	>35
Urine o/p (ml/hr)	>30	20-30	5-15	negligible
Treatment	crystalloid	crystalloid	crystalloid + blood	Crystallloid + blood

SIRS and Septic Shock

Systemic inflammatory response syndrome (SIRS)

is a general inflammatory response to various causes. It is considered to be due to cytokines (cytokine storm)

SIRS can be diagnosed when **two or more of the following are present**

- (1) Heart rate > 90 beats per minute
- (2) Body temperature < 36 or > 38°C
- (3) Hyperventilation (high respiratory rate) > 20 breaths per minute or, on blood gas, a PaCO₂ less than 32 mm Hg
- (4) White blood cell count < 4000 cells/mm³ or > 12000 cells/mm³, or the presence of greater than 10% immature neutrophils.

SIRS + proof of infection = sepsis

Sepsis + tissue hypoperfusion = septic shock

Inflammatory Response

Immune response

Shock

Questions?

Wound Healing

Haematology MCEM A

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NIHR Academic Clinical Lecturer in Emergency Medicine
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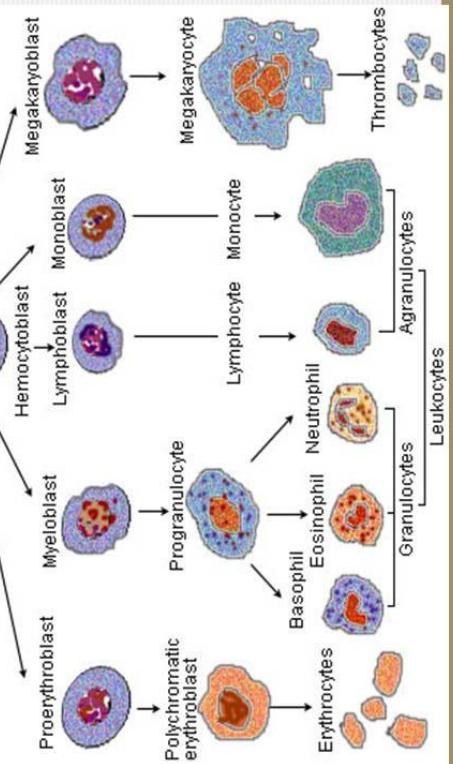
Syllabus

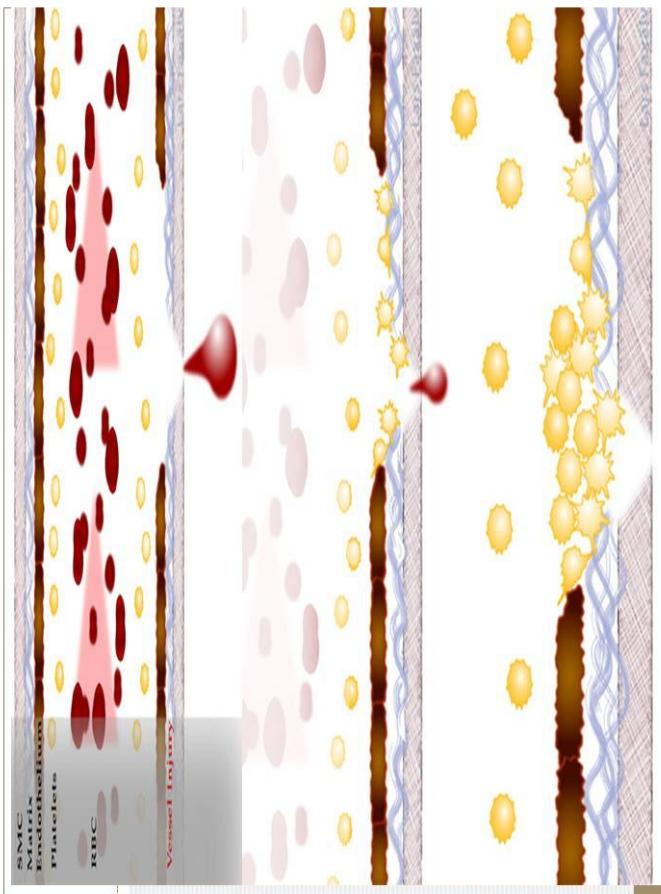
- Erythropoiesis
- Blood groups
- **Coagulation**
- Thrombolysis
- FBC components
- Reticulocytes
- Bleeding time
- Coagulation
- Specific clotting factors
- Iron
- Vitamin B12 & folate

Haemostasis

- Haemorrhage arrested following vascular injury.
- Vessel wall
- Platelets
- Coagulation Factors.

Haemopoiesis





Disorders of haemostasis – Vessel Wall abnormalities

- Easy bruising, purpura, spontaneous bleeding from mucosal surfaces.
- Bleeding time, PT, APTT, Plt count: Normal

Inherited:

- Hereditary haemorrhagic telangiectasia.
- Ehlers Danlos.
- Marfans.

Acquired:

- Vitamin c deficiency
- Steroid therapy
- Immune complex deposition eg sepsis



Platelets

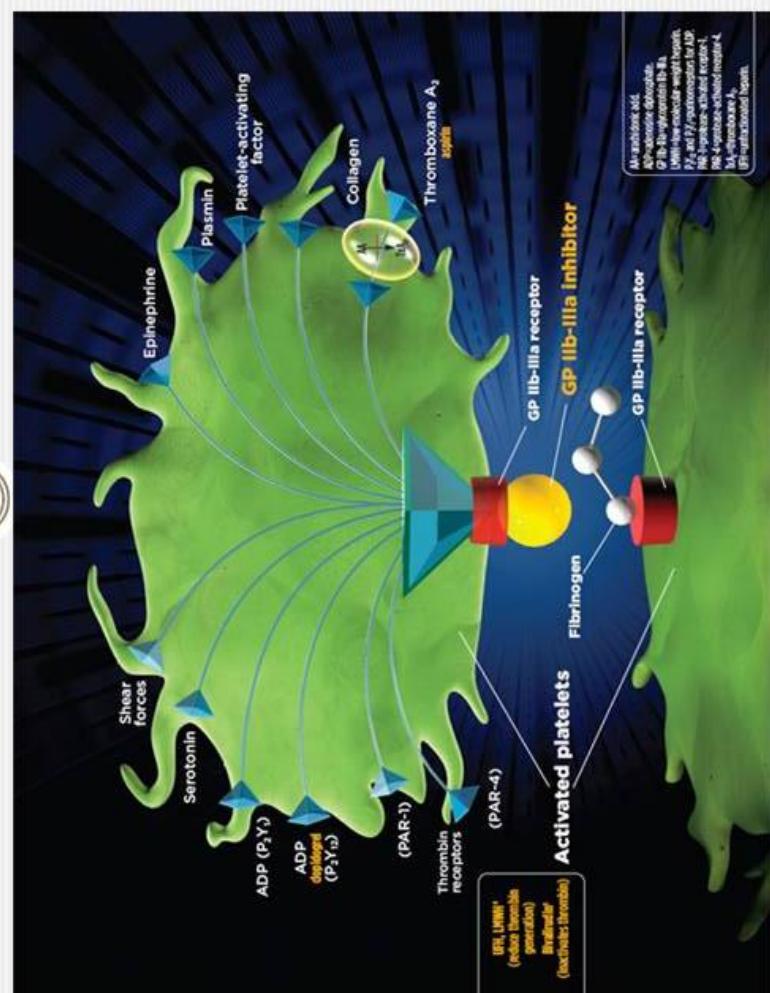
- Megakaryocytes (MK): multinucleated cells derived from stem cells in BM.
- Platelets break off from MK cytoplasm and enter blood.
- Thrombopoietin stimulates production.
- Life span 7-10 days then destroyed in spleen or pulmonary vascular bed.

- Express HLA Class I antigens on surface

Role of platelet in haemostasis

- Cross-linking collagen through GPIIb/IIIa receptors with fibrinogen
 - Factor VIII and Von Willebrand Factor
 - Express HLA Class I antigens on surface
 - TXA2 and ADP involved in platelet activation
 - Role of platelet inhibitors

Platelet Inhibition



Antiplatelet Activity

Mechanism	Drug
Cylooxygenase inhibitors	Aspirin
ADP receptor inhibitor	Clopidogrel, Prasugrel
Phosphodiesterase inhibitor	Cilostazol
Glycoprotein IIB/IIA inhibitors	Abciximab, Tirofiban
Adenosine reuptake inhibitor	Dipyridimole

Disorders of haemostasis - platelets

Congenital:

- Wiskott-Aldrich syndrome.
- Congenital rubella
- Congenital CMV

Acquired:

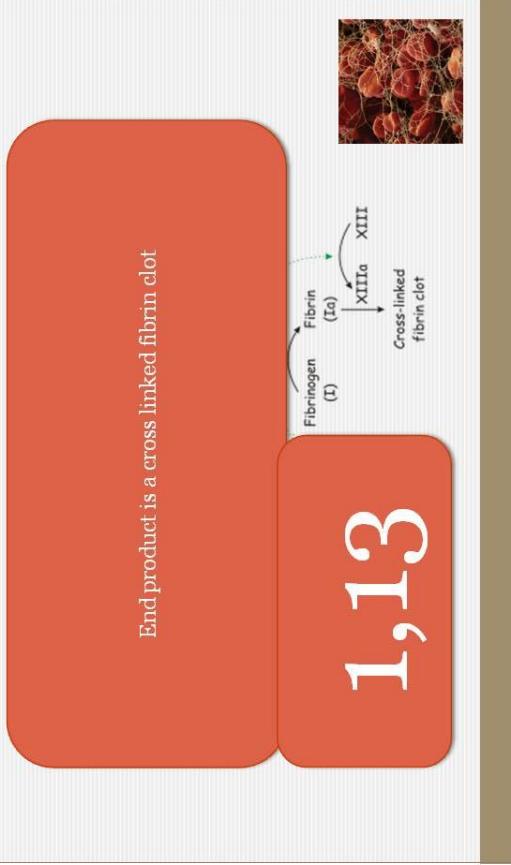
- ITP:
childhood.
Post viral infection
- Drugs:
Heparin
Quinine

Question

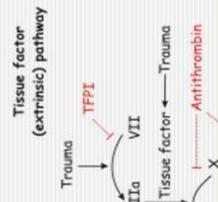
The following are true of platelet aggregation in thrombosis

- a. thromboxane A₂ stimulates platelet activation
(T)
- b. glycoprotein IIb/IIIa receptors bind activated platelets to the walls of damaged blood vessels
(F)
- c. activated platelets express von Willebrand's factor (vWF) on their surface membrane
(F)
- d. clopidogrel and prasugrel irreversibly block platelet ADP receptors
(T)

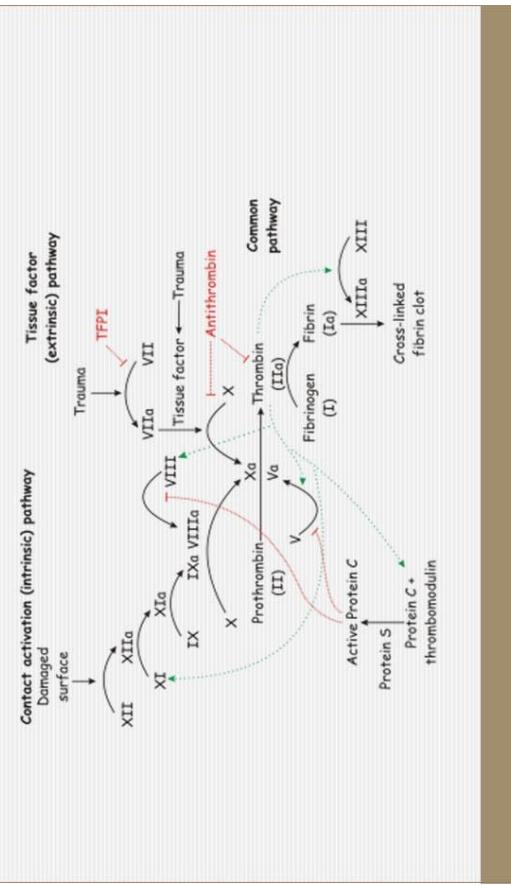
Clotting cascade



1,13



7



10,5



2

12,11,9,8

The diagram illustrates the coagulation cascade. It starts with the 'Contact activation (intrinsic) pathway' where Factor XII is activated by a 'Damaged surface'. This leads to Factor XIa activating Factor IX, which then activates Factor VIIIa. Factor VIIIa activates Factor IXa, which further activates Factor X. The 'Tissue factor (extrinsic) pathway' is triggered by 'Trauma', leading to Factor VIIa activating Factor X. Factor Xa then activates Factor Va and Factor VIIIa. The two pathways converge at Factor Va, which, along with Factor VIIIa, activates Factor II (Thrombin). Thrombin converts Factor fibrinogen (F) into Factor (Ia), which forms a cross-linked fibrin clot. Various inhibitors are shown: Antithrombin inhibits Factor Xa, Factor Va, and Factor IIa; Tissue factor Pathway Inhibitor (TFPI) inhibits Factor VIIa; and Protein C and Protein S inhibit Factor Va.

Tests of Coagulation

Blood Tests



- INR: testing extrinsic system
- APTT: testing intrinsic system

Investigation of bleeding disorders

- Platelets: ↓ do fbc, film, Bone Marrow.
- INR: ↑ look for liver disease, anticoagulant dx.
- APTT: ↑ consider factor VIII/IX deficiency or heparin.
- BT: ↑ consider vWD or Plt disorder.

Question

Disorder	INR	APTT	TT	Plt	Bleeding time
Liver Dx	↑	↑	↔	↔	↔↑
Plt defect	↔	↔	↔	↔	↑
Vitamin K deficiency	↑↑	↑	↔	↔	↔
Haemophilia	↔	↑↑	↔	↔	↔
Von Willebrand	↔	↑↑	↔	↔	↑
DIC	↑↑	↑↑	↑↑	↓	↑

Question

Regarding heparin and its role in anticoagulation

- a. Causes thrombocytopenia
True (heparin induced thrombocytopenia)
- b. APTT is a measure of the extrinsic clotting pathway
False (intrinsic)
- c. Exerts its anticoagulant effect through binding and activating thrombin and factor Xa
False (links between antithrombin and factors IIa, IXa, Xa, and XIa)
- d. In high dose can be used to lyse established thrombus
False (not effective for established thrombus)

Question

Appropriate function of the coagulation cascade requires

- a. Factor VIII binding to exposed collagen of damaged blood vessels
(F)
- b. Carboxylation of factors II, VII, IX and X by vitamin K dependent enzymes
(T)
- c. Conversion of fibrinogen to fibrin by plasmin
(F)
- d. Activation of protein C and protein S
(T)

Question

The following are true of platelet aggregation in thrombosis

- a. thromboxane A2 stimulates platelet activation
(T)
- b. glycoprotein IIIb/IIla receptors bind activated platelets to the walls of damaged blood vessels
(F)
- c. activated platelets express von Willebrand's factor (vWF) on their surface membrane
(F)
- d. clopidogrel and prasugrel irreversibly block platelet ADP receptors
(T)

Disorders of coagulation

Haemophilia A

Factor VIII deficiency

- X linked
- Haemarthroses & joint disease.
- Raised APTT, normal PT, normal bleeding time (BT) 3-8 mins
- Rx with factors infusion.
- Desmopressin.

Disorders of coagulation

Haemophilia B

- Factor IX deficiency.
- Similar clinical features to Haemophilia A
- X linked.
- 4 times less common.
- Desmopressin not effective.

Von Willebrand's Dx

- AD - vWF gene.
- Produced by endothelial cells at injury.
- Carries Factor VIII and mediates platelet adhesion.
- Mucosal bleeding.

- APPT prolonged, BT prolonged, PT normal.
- PFA-100 test for platelet function
- Rx: Intermediate purity factor VIII

Thrombosis

- Platelets and fibrin interact to form haemostatic plug thus vascular obstruction.
- Factor V Leiden (5% of population)
 - Protein C or S deficiency (these inhibit factors V and VIII)
- Anti thrombin deficiency
 - Antiphospholipid syndrome.



Red Cells / Erythrocytes

- The following clotting factors are vitamin K dependent
- a. Prothrombin

• **True**

• b. Factor VII

• **True**

• c. Factor XII

• **False**

• d. Protein C

• **True**

- Contain HB allowing O₂/CO₂ carrying.
- 4 polypeptide globin chains with iron containing haem molecule each RBC has 640 million units

• Hb F to Hb A switch at 3-6 months

• Hb A ($\alpha_1\beta_2$) 96-98%

• Hb F ($\alpha_2\gamma_2$) 0.5-0.8%

• Hb A₂ ($\alpha_2\delta_2$) 1.5-3.2%

- Mature red cells have no nucleus, ribosomes or mitochondria.
- 10^{12} produced daily, travel 480 km over a life span of 120 days
- Removed by macrophages in the reticuloendothelial system.

Question 4

- The following clotting factors are vitamin K dependent
- a. Prothrombin

• **True**

• b. Factor VII

• **True**

• c. Factor XII

• **False**

• d. Protein C

• **True**

Erythropoietin

- A hormone that controls the production of red cells
- Produced in Kidney (90%) liver and elsewhere (10%)
- No preformed stores
- Stimulates erythroblasts to proliferate and differentiate via transcription factors GATA-1 and FOG-1
- EPO production increased by hypoxia and anaemia
- Used for treatment anaemia associated with
 - chronic renal disease
 - Myelodysplastic syndrome
 - HIV,
 - Chronic disease
 - The Lancoprotein for improving race outcomes



Question

Erythropoietin

a. Is a cytokine

False (it's a hormone)

b. Is released from the peritubular fibroblasts of the bone marrow

False (90% kidney 10% liver)

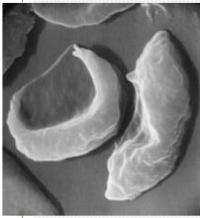
c. Stimulates maturation of normoblasts into reticulocytes

True

d. Is upregulated by persistent hypoxia and **hypoxia**

False (affected by anaemia and hypoxia)

Anaemia



- Hb < 13 g/dL adult male
- Hb < 12 g/dL adult female
- Hb < 11.5 g/dL (age 2-14)
- WHO reference

- Changes in plasma volume may mask anaemia
- Dehydration /polycythaemia/ pregnancy

Question

Investigation of tiredness in an otherwise well 60yr old patient reveals the following full blood count results : Hb 7.1, WCC 6.4, platelets 256, MCV 114.

- a. The anaemia results from a failure of DNA synthesis
True macrocytic anaemia with raised MCV
- b. A deficiency of intrinsic factor is the most likely cause of the abnormal results
True (pernicious anaemia, gastrectomy)
- c. This patient should be treated with blood transfusion
False (correct B₁₂ and folate levels)
- d. Where folate deficiency is the cause folate alone is the treatment
False (folate without B₁₂ may aggravate neurological features)

Question

The following may be the cause of anaemia in a patient with haemoglobin 7.9 and MCV 116

- a. myelodysplastic syndrome
(T)
- b. renal failure
(F)
- c. phenytoin therapy
(T)
- d. hyperthyroidism
(F)

Normocytic anaemia

- MCV 80-95 fL
- MCH >27 pg
- Haemolytic anaemia
 - Chronic disease
 - Acute blood loss (takes a day to show)
 - Bone marrow failure (chemotherapy, malignancy)
- Associated with pancytopaenia

Iron



- 10-15mg of iron daily.
- 1mg daily loss.
- 10% absorbed through duodenum.
- Ferrous ($2+$) $>$ ferric ($3+$) absorption.
- Iron deficiency:
 - Blood loss.
 - Malabsorption.
 - Poor dietary intake.

Microcytosis

- MCV $<$ 80 fL
- MCH $<$ 27 pg:
 - Iron deficiency anaemia.
 - Thalassaemia (MCV disproportionately low)
 - Congenital sideroblastic anaemia
 - Lead poisoning

Macrocytic Anaemia (MCV $>$ 95 fL)

- **Non- megaloblastic**
 - Myelodysplastic Syndromes.
 - Reticulocytosis
 - Drugs eg phenytoin, azothioprine, hydroxyurea
 - Alcohol
 - Liver disease
- **Megaloblastic**
 - B_{12} /folate deficiency
 - Abnormal B_{12} or folate metabolism
 - Defect of DNA synthesis
 - Antifolate drugs
 - Nitrous oxide

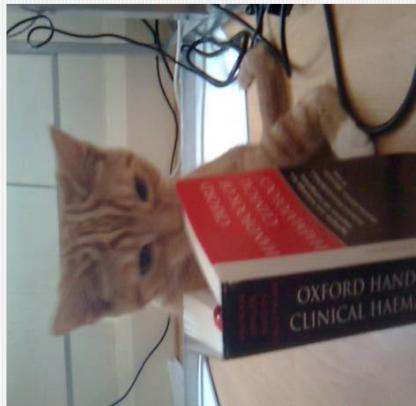
B_{12} & Folate



Folate Deficiency

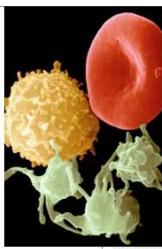
- Pernicious Anaemia.
- Post gastrectomy.
- Vegans.
- Terminal ileum dx:
 - Crohn's, blind loops, diverticula.
- Increased need:
 - Pregnancy
 - Haemolysis
 - Malignancy

More in your handout



Transfusion ABO

Phenotype	O ⁺	A ⁺	B ⁺	AB ⁺	O ⁻	A ⁻	B ⁻	AB ⁻
UK percentage	37	35	8	3	7	7	2	1
Geneotype	OO	AA AO	BB BO	AB				
Antigens present	none	A	B	AB				
Antibody (IgM)	Anti A Anti B	Anti B Anti A	Anti A Anti B	none				
Transfusion					UD		UR	



Haemolysis

- Red cells destroyed in marrow, liver and spleen after 120 days
- Production of RBC can increase 8 fold in marrow to compensate
- Hereditary "intrinsic" red cell defects**
- Acquired "environmental" causes**
- Increased RBC breakdown** (increased bilirubin, urobilinogen, fecal stercobilinogen, depleted haptoglobins)
- Increased RBC production** (reticulocytosis, bone marrow hyperplasia)
- Damaged cell morphology** (spherocytes, elliptocytes, fragments)

Question 5

- The following statements are true of the blood grouping
 - a. Persons with blood group O can donate blood to individuals of any ABO blood group (universal donor) but receive blood only from a group O individual
 - **True**
 - b. Donors with blood group B will carry antibodies to the A antigen in their serum
 - **True**
 - c. Maternal anti-RhD antibodies can pass across the placenta
 - **True**
 - d. Donor platelets must be screened for ABO compatibility but not Rh compatibility
 - **False**

HA: Hereditary causes

- Membrane
 - Spherocytosis
 - Elliptocytosis
- Metabolism
 - G6PD deficiency
 - Pyruvate Kinase deficiency
- Haemoglobin
 - Sickle
 - Thalassaemia

HA: Acquired causes

Warm

- Alloimmune: Haemolytic disease of newborn, haemolytic transfusion reactions, marrow transplants, drug red cell complexes
- Autoimmune : Idiopathic, SLE, CLL, lymphoma, methyldopa

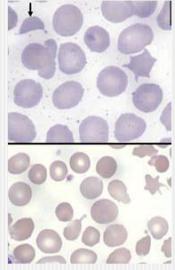
Cold

- Paroxysmal nocturnal haemoglobinuria.
- Infections: mycoplasma pneumonia, infectious mononucleosis

Question

A patient with a haemolytic anaemia may also have

- a. Helmet cells seen on the blood film **True**
- b. Jaundice **True**
- c. A +ve direct Coombs test **True**
- d. Sternotomy scar **True**



Question

The following are true of pathology of red blood cells

- a. positive direct coombs test indicates a non-immune cause of red cell haemolysis (F)
- b. glucose-6-phosphate (G6PD) deficiency causes bouts of haemolytic anaemia following exposure to oxidative stress (T)
- c. helmet cells are seen in the blood of patients with methaemoglobinemia (F)
- d. aged and damaged red blood cells are removed by the bone marrow (F)

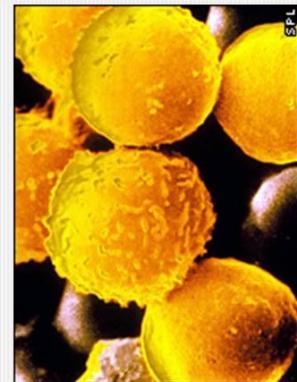
Red Cell Abnormalities (I)

- **Macrocyte:** Liver disease, alcoholism
- **Microcyte:** Fe deficiency haemoglobinopathy
- **Target cell:** Fe deficiency, liver disease, post splenectomy haemoglobinopathies
- **Pencil cell:** Fe deficiency
- **Howell Jolly body:** Post splenectomy/ hypoplasplenism
- **Acanthocyte:** Abetalipoproteinemia, renal failure
- **Fragments:** DIC, microangiopathy, HUS, TTP, cardiac valves, burns
- **Stomatocyte:** Liver disease, alcoholism

Red Cell abnormality (II)

- **Echinocyte:** Liver disease, post-splenectomy, artefact
- **Acanthocyte:** liver disease, abetalipoproteinemia, renal failure
- **Tear drop:** Myelofibrosis, extramedullary haemopoiesis
- **Basket cell:** Oxidative damage, G6PD deficiency
- **Microspherocyte:** Hereditary spherocytosis, autoimmune haemolytic anaemia, sephicaemia
- **Basophilic stippling:** Pb poisoning, myelodysplasia, haemolytic anaemia
- Change in shape (**poikilocytosis**) and size (**anisocytosis**) found in many anaemias (DIC, G6PD, HUS, TTP)

Haematological Malignancies



- Leukaemias
- Acute myeloid
- Acute lymphoblastic
- Chronic myeloid
- Chronic lymphoblastic

Acute Leukemia

- Haemopoietic blast cells >30% of BM.
- 1000 new cases of ALL & AML each/yr.
- Short histories:
 - anaemia, bruising,
 - Sweating, fevers, general malaise.
 - LN, hepatosplenomegaly.
- Labs:
 - Anaemia
 - Thrombocytopenia
 - Neutropenia

ALL prognostic signs

Poor prognosis

- Philadelphia translocation t(9;22) increases with age
- Boys
- Adult or infant <2 yrs
- WCC $> 50 \times 10^9/L$
- T- ALL Cell phenotype
- Time to remission > 4 weeks
- CNS involvement at presentation

Good prognosis

- TEL arrangement
- Girls
- Children
- Low WCC count
- Time to remission < 4 weeks
- Absent CNS disease at presentation

Question

- With regard to the leukaemias
- a. Acute lymphoblastic leukaemia (ALL) is primarily an adult disease
- **False**
- b. The philadelphia chromosome is present in 95% cases of acute myeloid leukaemia (AML)
- **False**
- c. Enlarged rubbery lymph nodes are a feature of chronic lymphocytic leukaemia (CLL)
- **True**
- d. In chronic myeloid leukaemia (CML) the white cell count may exceed $100 \times 10^9/L$ before any specific symptoms appear
- **True**

Regarding Hodgkin's lymphoma

- a. B symptoms include weight loss and night sweats but not pain from lymph node enlargement (T)
- b. is rare under the age of 60 (F)
- c. Reed sternberg cells are found in the blood (T)
- d. Ann Arbor stage III means involvement of lymph nodes on both sides of the diaphragm (T)

Neuroanatomy & Neurophysiology



For the MCEM part A

Giles Cattermole BM BCh FCEM
Consultant in Emergency Medicine
Princess Royal University Hospital

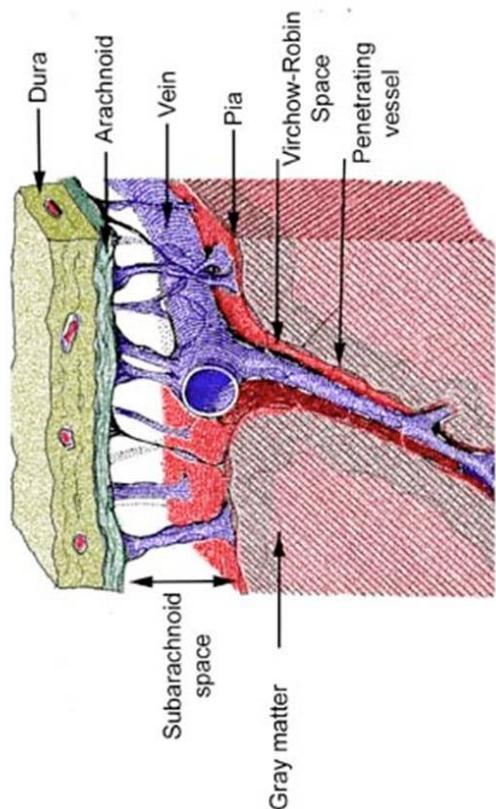
Key topics

Aug 2010 Basic sciences curriculum

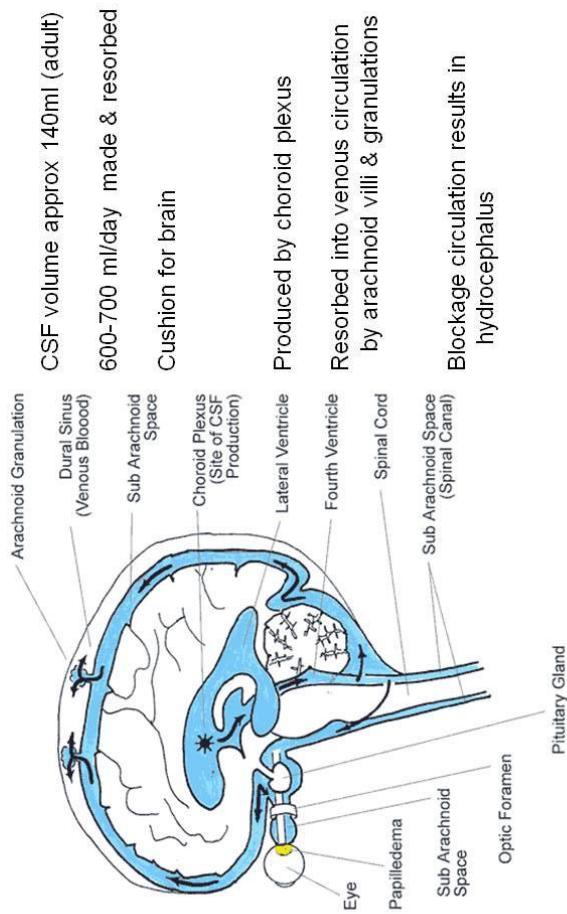
Central nervous system

- Arterial supply, venous drainage and CSF circulation
- Functional anatomy of the brain
 - Cranial nerve lesions and visual pathways
 - Spinal cord anatomy and cord lesions
 - Pain (mechanism and control)

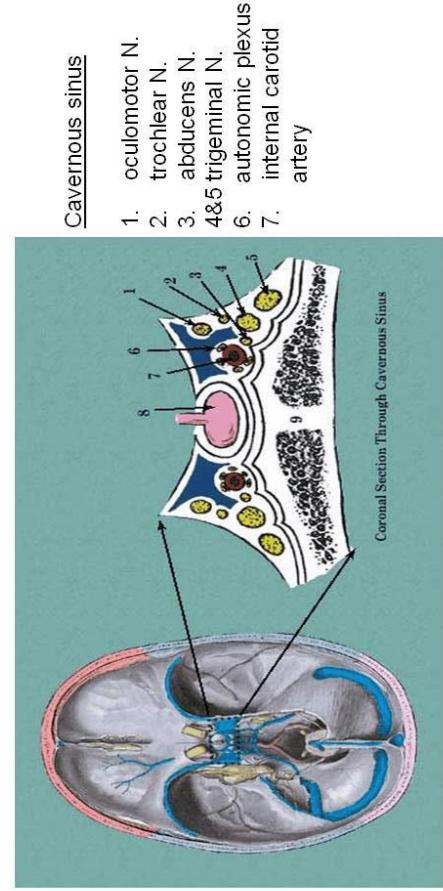
Meninges



Circulation CSF

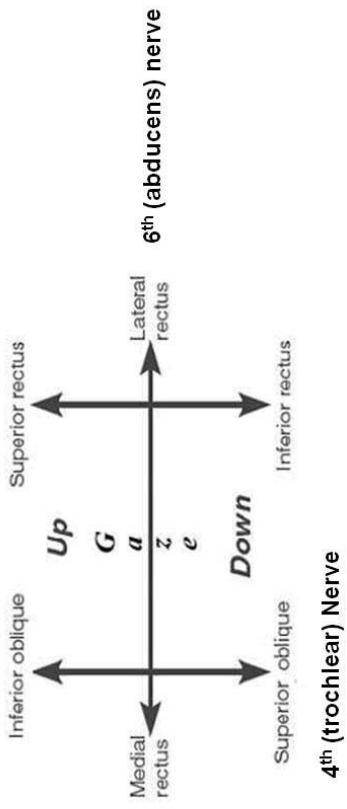


Venous circulation



Venous sinuses are venous channels within dura mater
Receive blood from internal and external veins of the brain
Ultimately drain blood into internal jugular vein

Control of eye Movements

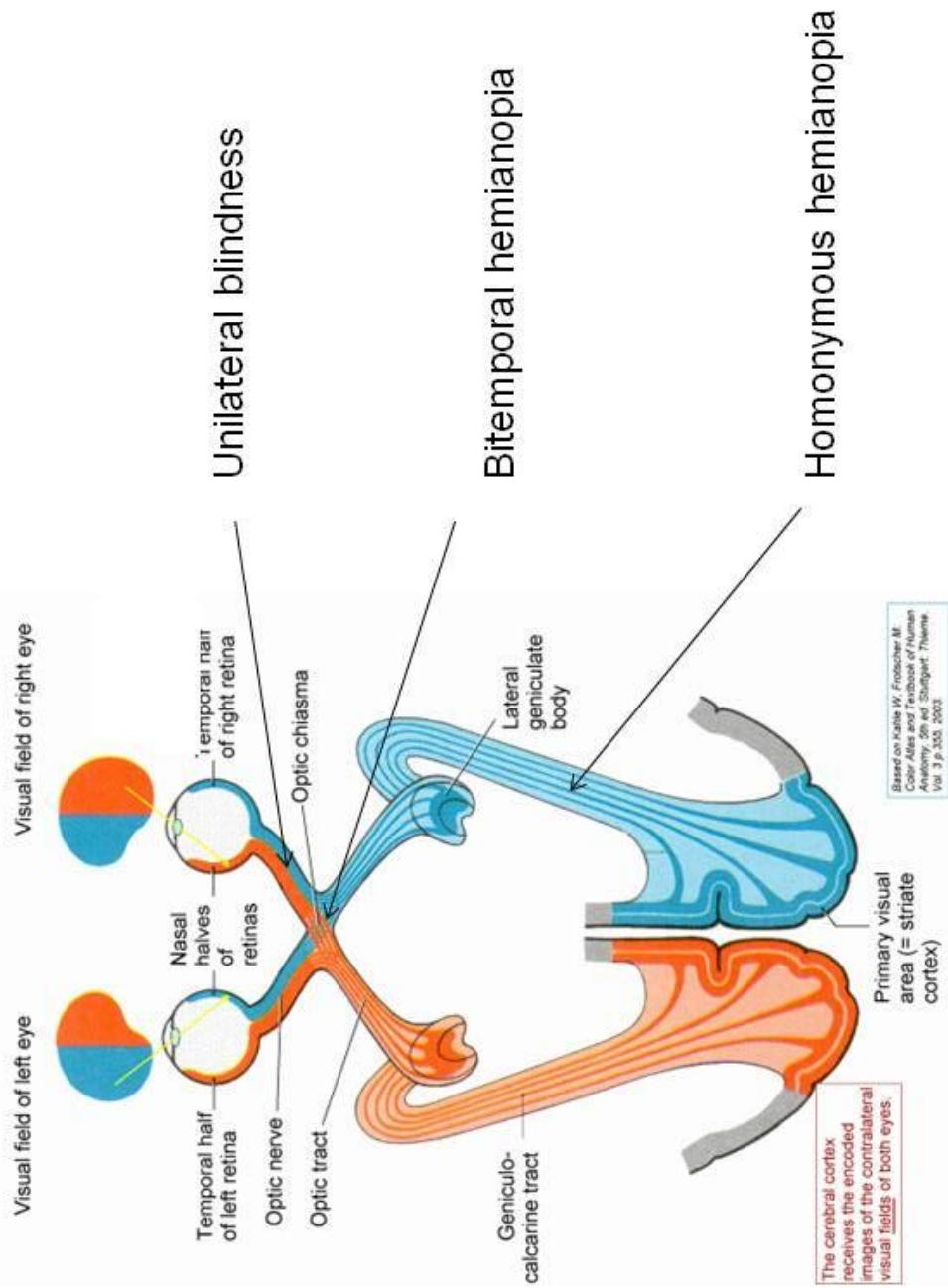


3rd (oculomotor) nerve – all the others

Oculomotor nerve palsy

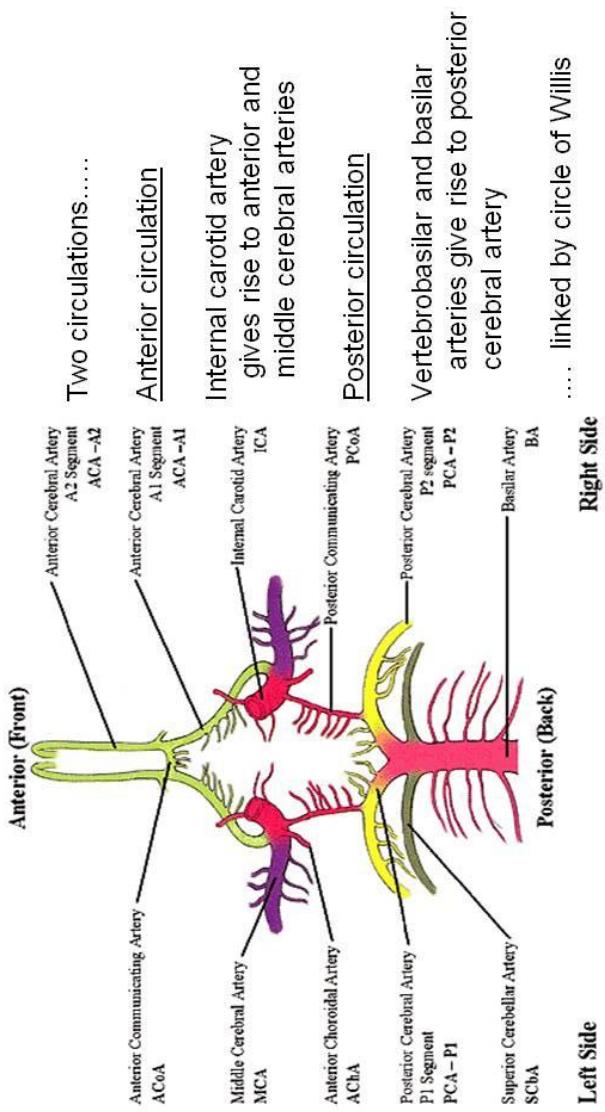
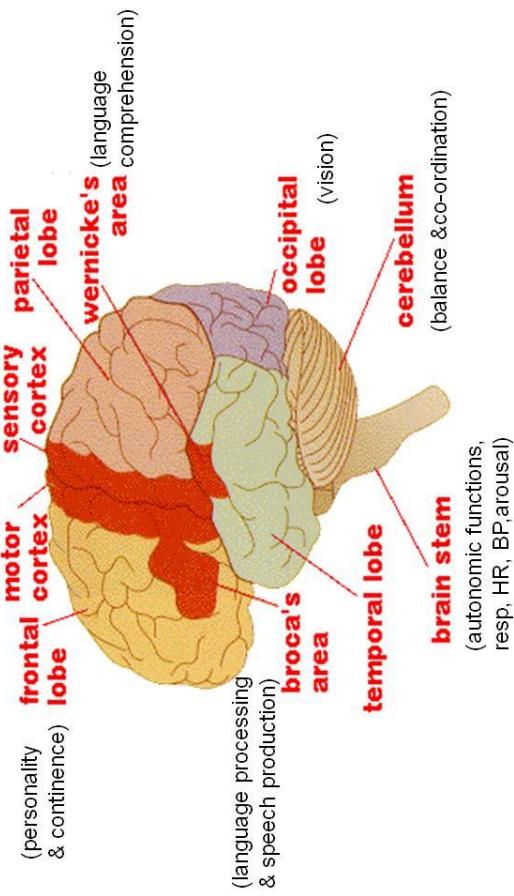


Visual Pathways

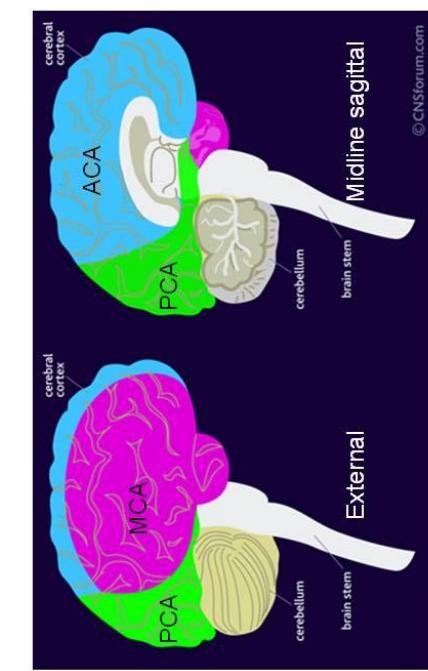


Arterial Supply to the Brain

Functional Anatomy of the Brain



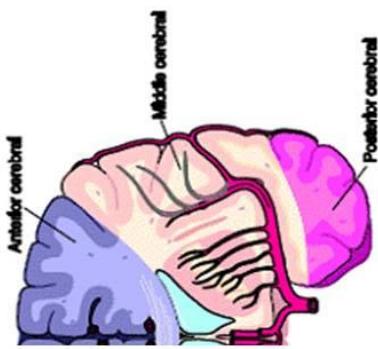
Arterial territories of the Brain



Internal carotids (incl. ACA and MCA) supply anterior 2/3rds cerebrum

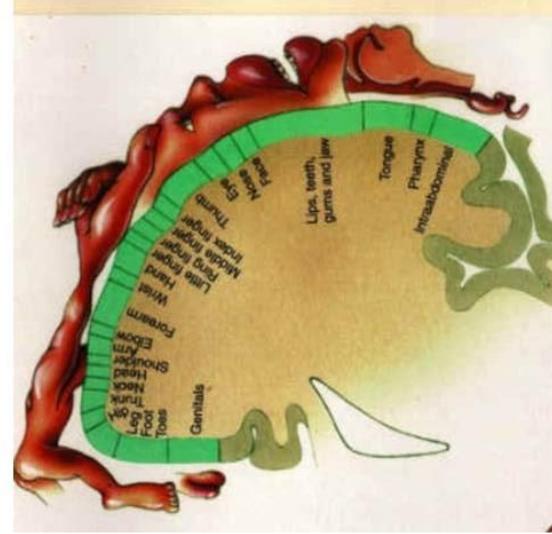
Vertebrabasilar arteries (incl. PCA) supply posterior 1/3 cerebrum, cerebellum and brain stem

Motor cortex

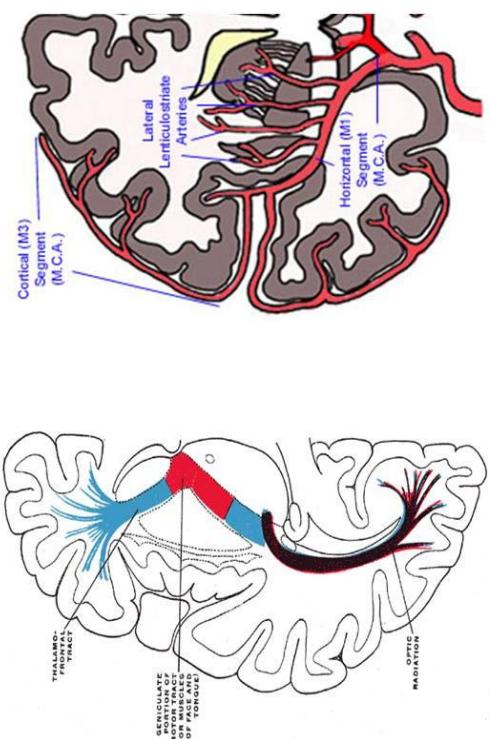


Anterior cerebral artery deficit
tends to affect leg > arm & face

Middle cerebral artery deficit
tends to affect face & hand > leg



Vascular Lesions of the Brain I



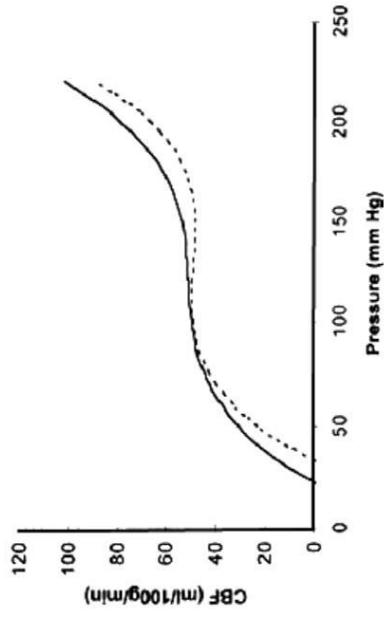
Proximal MCA occlusion gives hemiparesis (UL = LL) and homonymous hemianopia

Vascular Lesions of the Brain II

Anterior Circulation	Posterior Circulation
hemiparesis	hemiparesis
homonymous hemianopia	homonymous hemianopia
amaurosis fugax	cerebellar
dysphasia (if dominant lobe)	nystagmus, ataxia,
personality changes	scanning dysarthria
	brainstem
	vertigo, nausea, nystagmus
	eye signs
	bilateral weakness
	various syndromes

Control of Cerebral Blood Flow

Autoregulation maintains CBF constant for MAP 60-150mmHg



Control of Cerebral Blood Flow

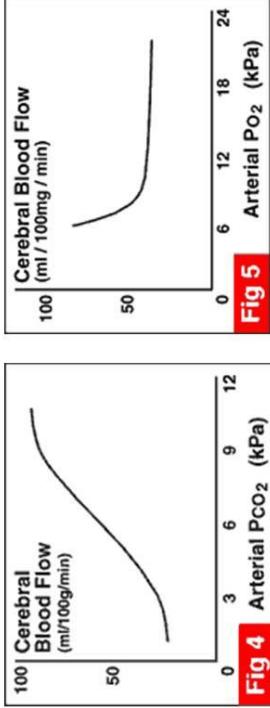


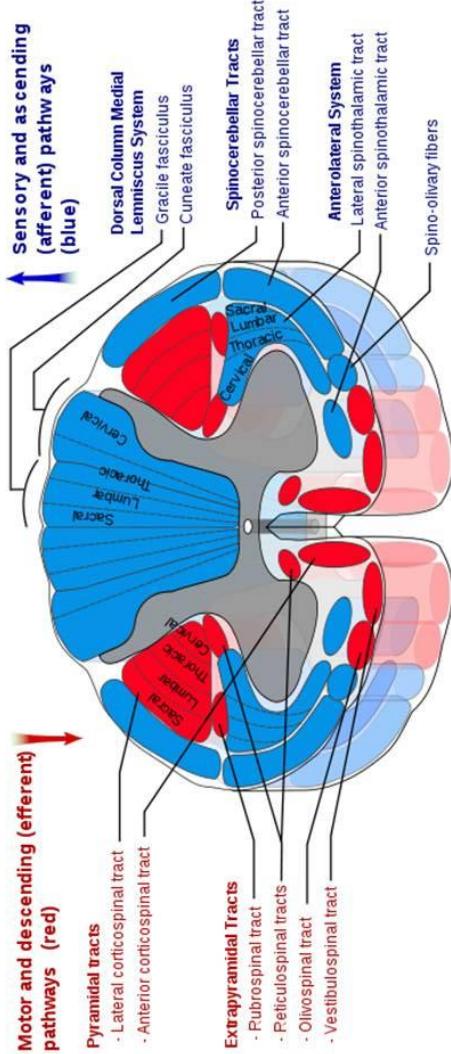
Fig 4

Fig 5

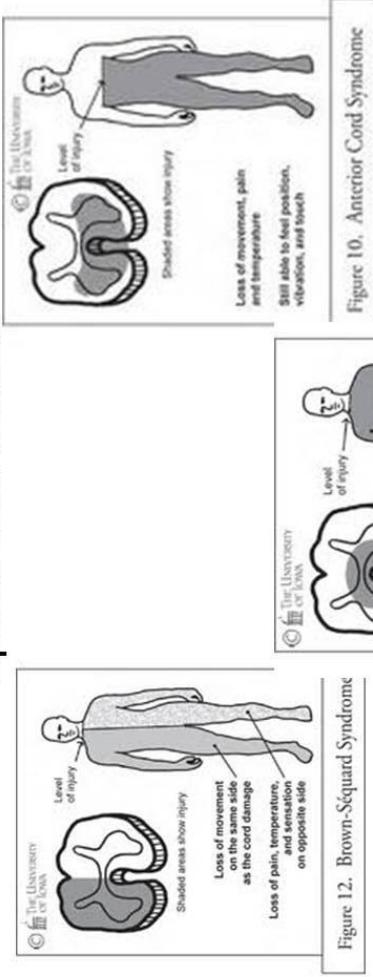
Local vasodilator metabolites : $\text{CO}_2/\text{H}^+/\text{K}^+$

Increased vasoconstrictor (sympathetic) tone allows constant for CBF at higher arterial pressures.

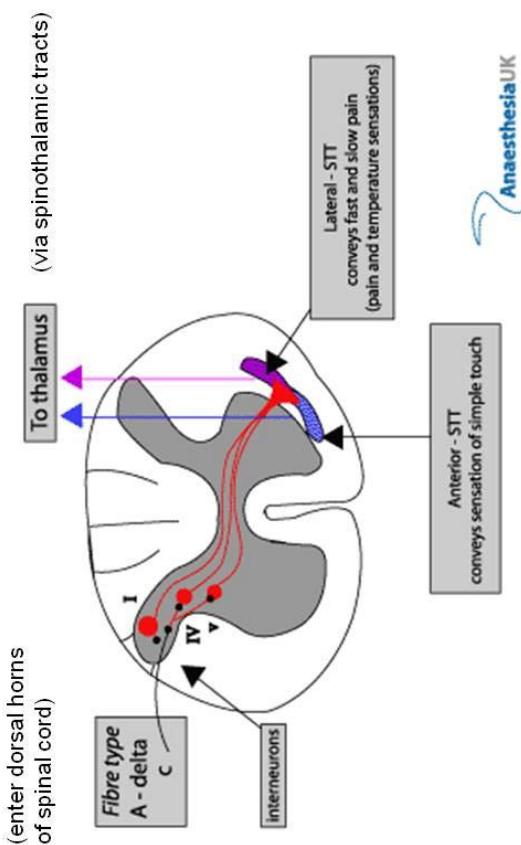
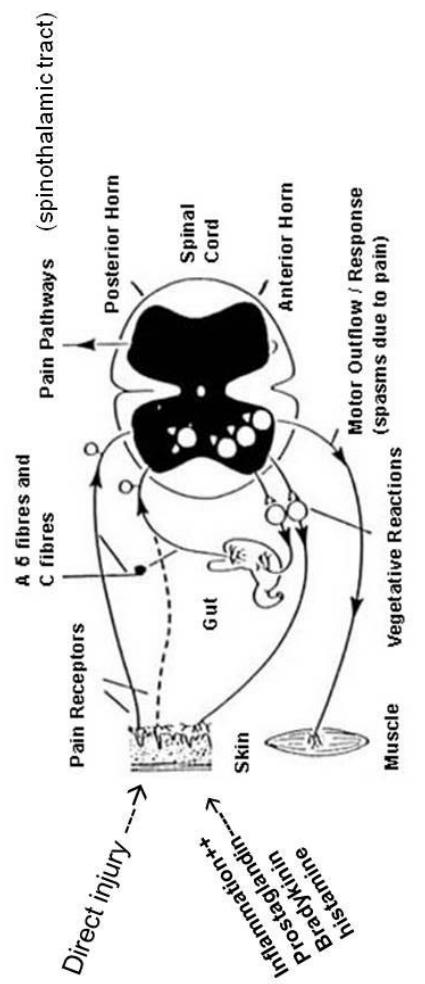
Spinal cord anatomy



Spinal cord lesions

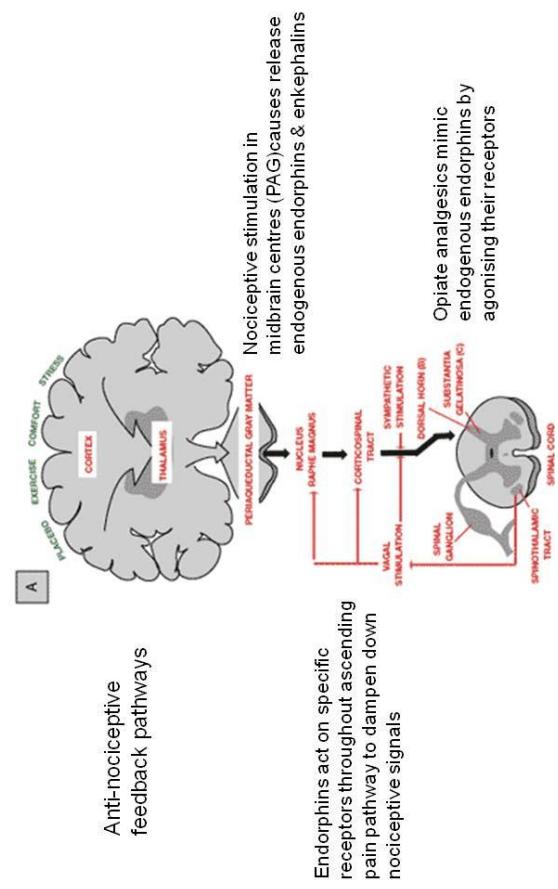
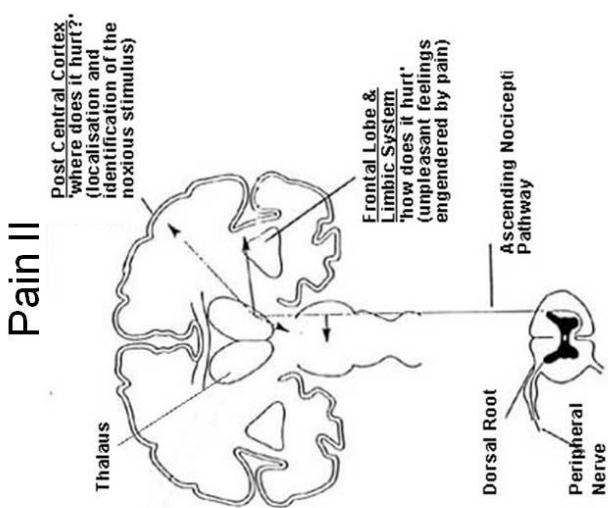


Pain



A-delta fibres – fast myelinated nerves with nociceptor endings in skin
 C fibres slow unmyelinated nerve endings in all tissues except CNS

Pain II

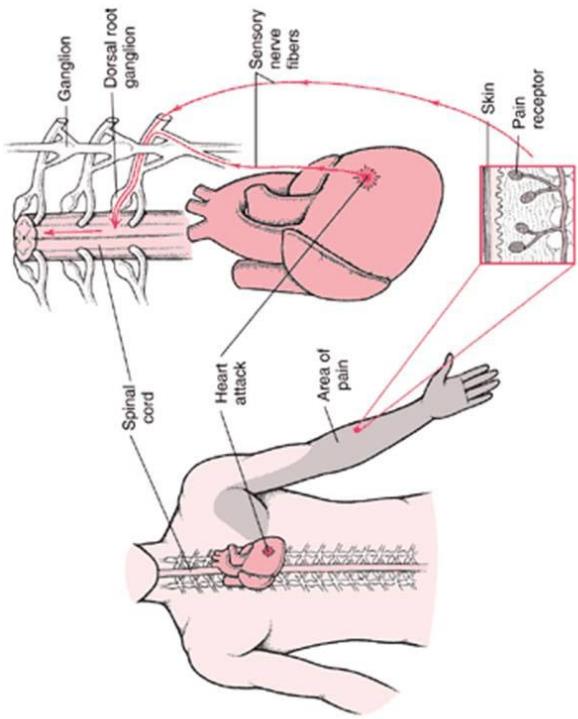


Pharmacology of Pain

Points of analgesic action

1. Reduce nociceptive stimulation by reducing inflammation (aspirin, NSAIDs)
2. Stimulate antinociceptive pathways which modify pain transmission (opiates)
3. Block transmission nociceptive nerve fibres (local anaesthetics)
4. Central action to reduce emotional component pain (morphine, antidepressants)

Referred Pain





Cardiovascular Physiology for MCEM Part A

Mathew Hall PhD MCEM
Specialty Doctor
PRUH

(with slides from Pratik Sinha
ED & ICU Trainee
Imperial College)

What is expected I?

- **Cardiac electrophysiology**
 - Cardiac action potential, chronotropy & impulse conduction
 - ECG basics
 - ECG abnormalities (axis deviation, bundle branch blocks, heart blocks, tachyarrhythmia, ischaemia)
 - Electrolyte abnormalities and the heart
- **The cardiac pump**
 - Frank Starling relationship
 - Preload, afterload and contractility
 - Heart failure
- **The cardiac cycle (electromechanical cycle of the heart)**
 - *Cardiovascular examination in relation to the cardiac cycle (HS, murmurs, JVP etc)*



What is expected II?

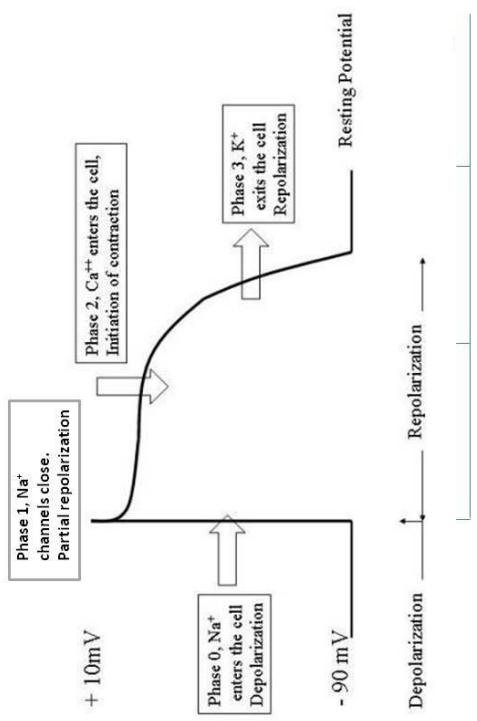
- **Peripheral vascular physiology**
 - Vascular resistance
 - *Blood flow through various tissues and organs*
- **Cardiovascular regulation**
 - Control of heart rate
 - Control of mean arterial pressure
- **The microcirculation**
 - *Anatomy of the microcirculation*
 - *Starlings forces and fluid movement across the capillary membrane*



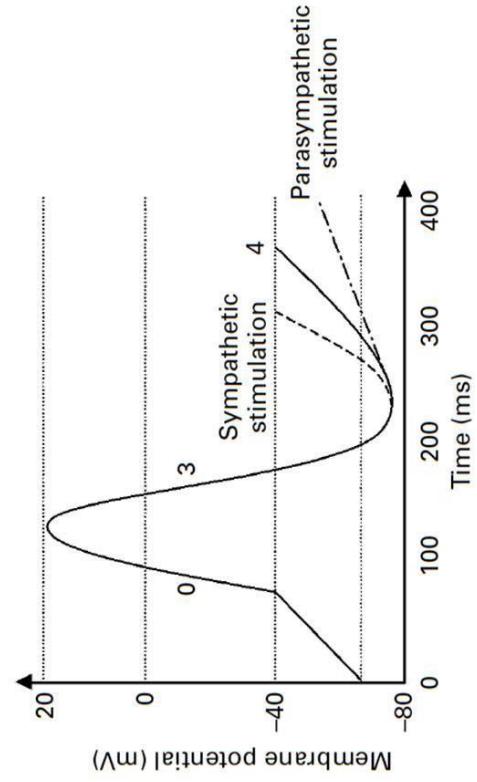
Cardiac muscle



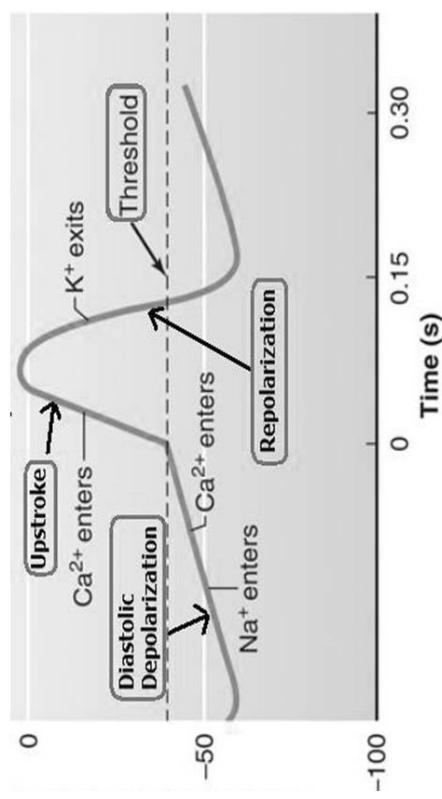
Myocyte action potential



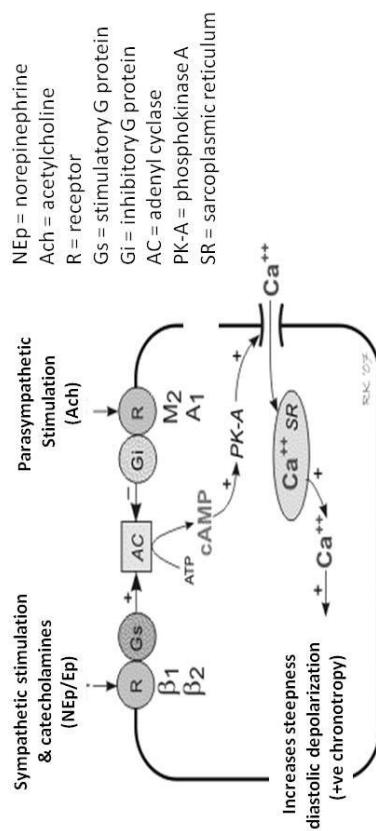
Automaticity



Pacemaker potential (SA nodal cells)

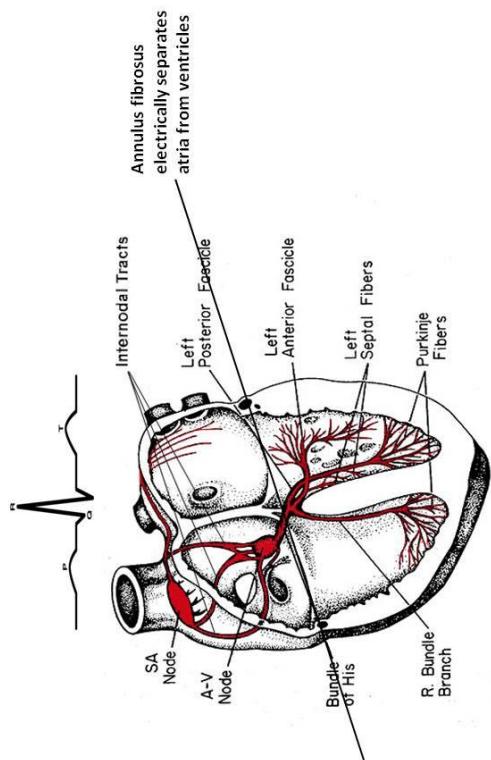


Chronotropy

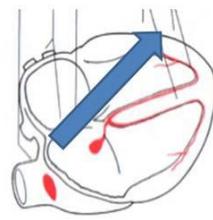




Impulse conduction



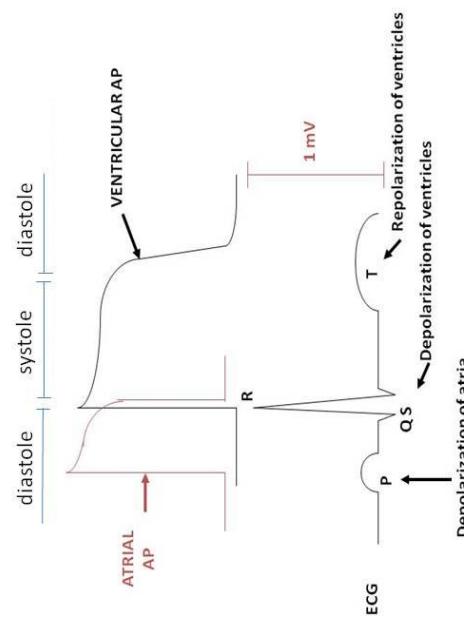
Einthoven's triangle



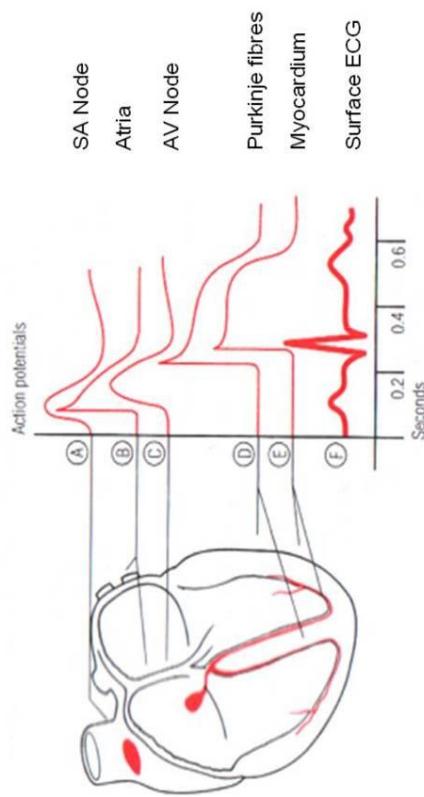
- Lead I: -ve RA → LA +ve
- Lead II: -ve RA → LF +ve
- Lead III: -ve LA → LF +ve



Single action potential



Impulse conduction & the ECG



ECG

- Know the basics
 - Speed
 - Calibration
 - Intervals
 - PR (120 to 200ms)
 - QRS (80 to 120ms)
 - QT (300 to 430ms)- Know the correction for QTc
 - J point
 - Axis

ECG Axis

Left axis deviation

- Left ventricular hypertrophy
- Left anterior fascicular block

Normal axis (-30° to +90°)

Right axis deviation

- Left posterior fascicular block
- Right ventricular hypertrophy
- Chronic lung disease (COPD)
- Acute RV strain (PE)

ECG MI Diagnosis

ECG Lead	Wall Segment
V1-V4	Anterior Wall (LAD)
V1-V2	Anteroseptal (LAD)
V4-V6	Anterolateral (LCx)
I, aVL	Lateral Wall (LCx)
II, III, aVF	Inferior Wall (RCA)
V1-V2	True Posterior (LCx)

ECG changes of Myocardial infarction

Chest (precordial leads)

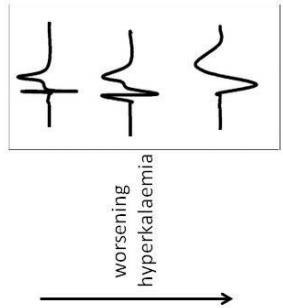
Causes of an upright R wave in V1

- RBBB
- Posterior MI
- Right ventricular hypertrophy



Electrolyte abnormalities

- Hyperkalaemia**
 - tall, tented narrow T waves
 - decreased P wave amplitude
 - widened QRS complexes
 - AV block
 - absent P waves
 - very broad, bizarre QRS complexes/sinusoidal appearance
 - VT/VF or ventricular asystole.
- Others**
 - hypokalaemia – (widening T waves, prolonged PR interval, ST depression, U waves and ventricular ectopics – ultimately SVT/VT)
 - hypercalcemia (shortened QT)
 - hypocalcemia (prolonged QT)



Important medical conditions & the ECG

- Hypo/hyperthyroidism
- Hypothermia
- Poisons (tricyclics + others)
- Differential diagnosis ST elevation
- Digitalis
- PE
- SAH



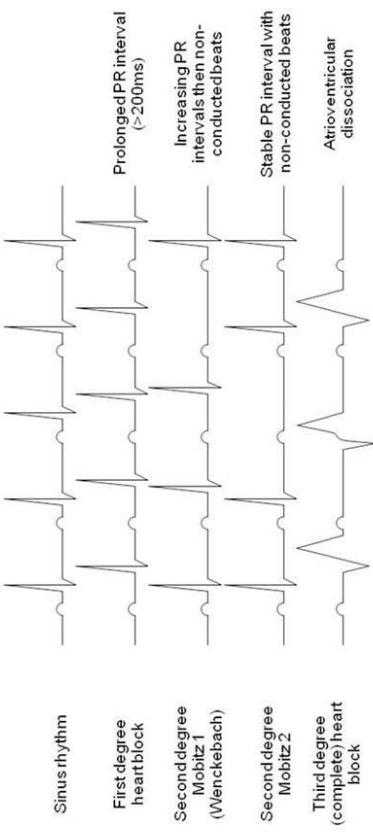
Arrhythmias

- AF
 - failure SA node (fibrosis, atrial dilatation, others)
 - chaotic atrial electrical activity
- AVNRT
 - irregular conduction to ventricle
 - re-entry circuit in right atrium, regular SVT
- WPW
 - accessory pathways atria-ventricles
 - shortened PR, slurred QRS upstroke (delta wave)
 - paroxysmal tachycardia
- VT
 - often circus rhythm around damaged myocardium
 - Polymorphic VT (Torsade)
 - prolonged QT (inherited, acquired – drugs)

(Difference between VT and SVT with aberrant conduction
- positive concordance across leads, capture beats, fusion beats)



Heart Block



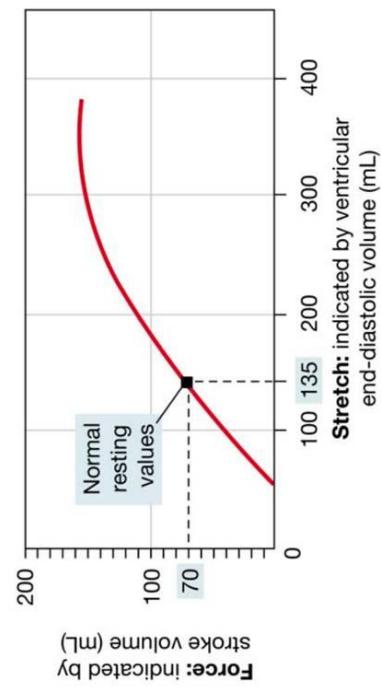


Cardiac output

- Cardiac Output = stroke volume x heart rate
- Heart rate is under autonomic control
- Stroke volume = volume blood ejected per ventricular contraction
 - Depends on 3 things
 - Preload
 - Afterload
 - Inotropy (contractility)



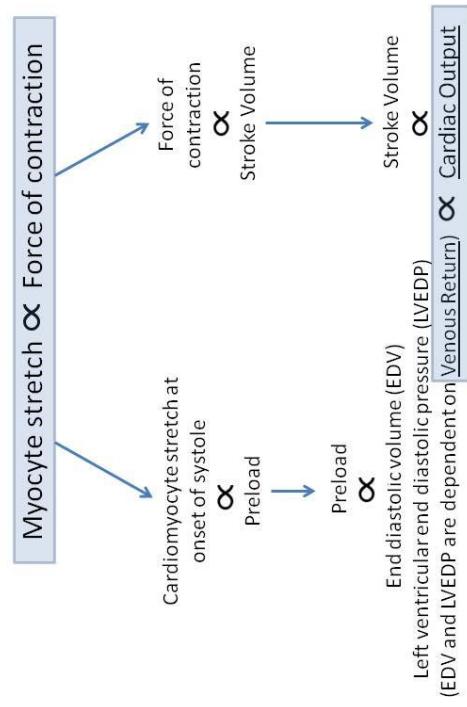
Frank-Starling Curve



The cardiac pump



Frank-Starling relationship



Afterload

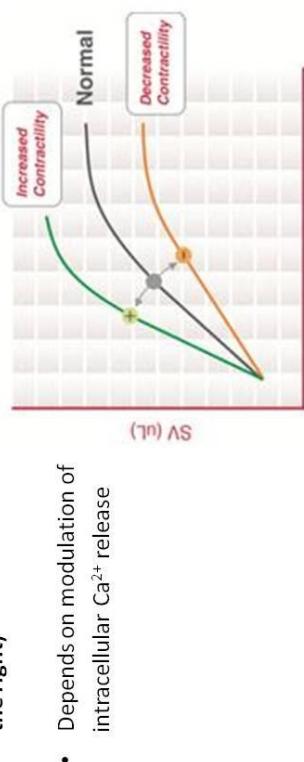
- Resistance to ventricular ejection
- In practice dictated by systemic vascular resistance (SVR)
- Gauged by mean arterial pressure (MAP)
- Increasing afterload reduces stroke volume**
- Not a big effect in the healthy heart, but increasingly important in the failing heart
- Increasing afterload also shifts Starling curve to the right

Inotropy (contractility)

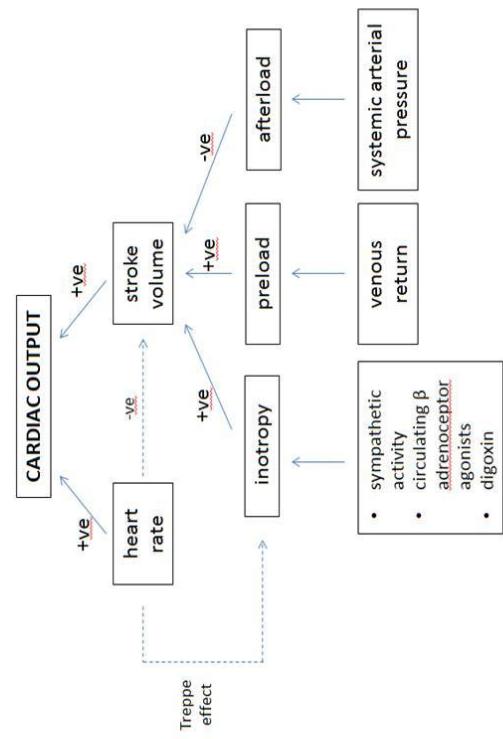
- Inotropy is increased by**
 - Sympathetic nervous stimulation
 - Circulating catecholamines (epinephrine, dopamine)
 - Positive inotropic drugs (digoxin, dobutamine, ephedrine)
- Inotropy is decreased by**
 - Cardiac failure
 - Acute cardiac ischaemia
 - Negatively inotropic drugs (beta blockers, calcium channel blockers)
 - Acidosis, hypoxia, hypercapnia

Inotropy (contractility)

- Ease of force (or power) generation by cardiac myocytes
- Easier force generation = greater force of contraction
- Increasing force of contraction (increased inotropy) increases stroke volume**) shifts the Starling curve to the left (decreased inotropy shifts to the right)



Control of cardiac output





Congestive cardiac failure

- LV dysfunction → LV failure → end stage HF
- Causes
 - Coronary artery disease (MI, ischaemia)
 - Hypertensive heart failure
 - Alcohol
 - Cardiomyopathy
 - Others
- Symptoms and signs
 - Left heart - dyspnoea, reduced exercise tolerance, orthopnoea, pulmonary oedema
 - Right heart – peripheral oedema, raised JVP, liver congestion
- Neurohormonal model
 - Initial injury → cardiac output (CO) reduced → compensation via increased sympathetic drive and up-regulation of the renin-angiotensin-aldosterone system
 - CO returns to normal BUT cardiac strain and angiotensin II cause ventricular remodeling over years → remodelled (hypertrophied) ventricle less effective than normal myocardium → CO reduces over time → further neurohormonal remodeling causes further declines in CO → vicious circle to end stage HF

Systemic Vascular Resistance

- Resistance to blood flow through the systemic circulation
- Systemic vascular resistance, **SVR = (MAP – CVP)/CO**
- Local arterioles are the primary determinant of SVR and the main source of resistance to blood flow to organs
- Modulated by
 - Sympathetic nervous system (α_2 receptors on vascular smooth muscle)
 - Circulating vasoactive hormones (angiotensin II, ADH, ANP)
 - Vascular endothelial factors (nitric oxide)
 - Non endothelial local factors (thromboxane, histamine)
 - Autoregulation (myogenic and metabolic mechanisms)
- Different organs and tissues regulate their vascular tone with specific combinations of the above modulators.

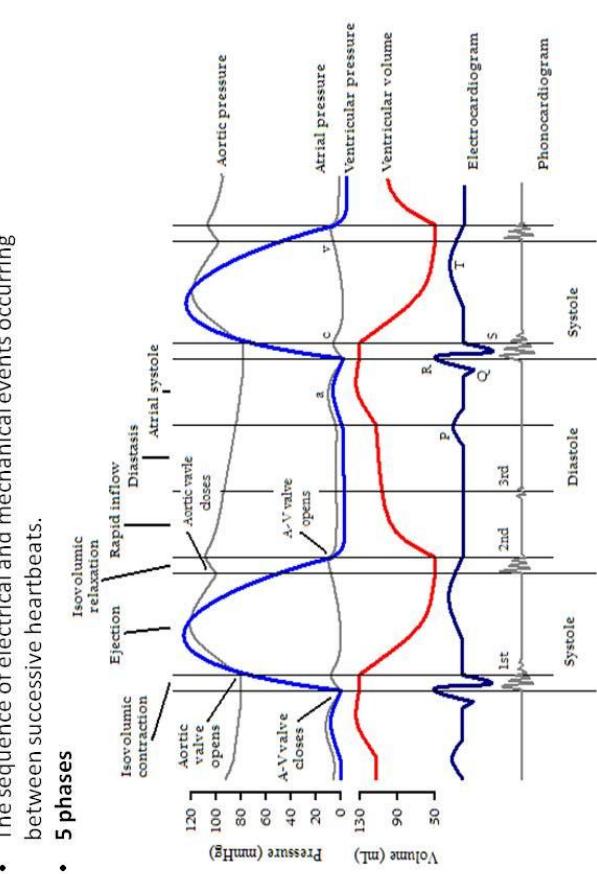


The cardiac cycle

- The sequence of electrical and mechanical events occurring between successive heartbeats.
- 5 phases
 - Isovolumic relaxation
 - Ejection
 - Rapid inflow
 - Diastasis
 - Atrial systole



The cardiac cycle





Cardiac cycle

Phase 1 – atrial contraction.

- Sino-atrial node depolarising spreads through both atria generating the P wave of the ECG. Atrial muscle contraction follows, expelling atrial blood into the ventricles to maximise venous return and complete ventricular filling. Only 20-30% of ventricular filling comes from atrial contraction – the **atrial 'kick'**. Peak atrial systolic pressures are around 10mmHg for the left atrium and 5mmHg for the right atrium. Phase 1 ends with ventricular contraction and the onset of systole. The volume of blood in the ventricles at the end of diastole (**the end-diastolic volume**) is typically 120ml.



Cardiac cycle

Phase 2. Isovolumetric ventricular contraction.

- Electrical depolarization spreads through the ventricular muscle generating the QRS complex of the ECG. The onset of ventricular contraction snaps shut the atrio-ventricular (AV) valves - mitral and tricuspid - preventing backflow of blood into the atria. Reverberation of blood following closure of AV valves generates the **first heart sound**. All four heart valves are now closed and pressure in the ventricles rises quickly without a change in ventricular volume (**isovolumetric contraction**). Aortic and pulmonary artery pressures have been steadily declining throughout diastole as the elastic recoil pushes blood forwards into the respective circulations. When right ventricular pressure rises above pulmonary artery pressures (around 5-10mmHg at this point) and left ventricular pressure rises above aortic pressure (80mmHg) the pulmonary and aortic valves open to allow ejection of blood.



Cardiac cycle

Phase 4. Isovolumetric ventricular relaxation.

- Semilunar valve closure generates the **2nd heart sound** - the aortic valve closes before the pulmonary valve leading to physiological splitting of the 2nd heart sound particularly evident during inspiration. Closure of the aortic valve gives a transient dip in arterial pressure felt as the '**dichrotic notch**' in the arterial pulse. All four valves are now closed again and the ventricles relax without change in volume (**isovolumetric relaxation**). Ventricular pressures plummet until they are near zero and below the pressure in the two atria (which have begun to fill with blood again). Isovolumetric relaxation ends with opening of the mitral and tricuspid valves and venous return into the ventricles.



Cardiac cycle

Phase 3. Ventricular ejection.

- The semi-lunar valves (aortic and pulmonary valves) are open and the ventricles contracting so that blood is ejected into the aorta and pulmonary arteries. Left ventricular pressure peaks at 125mmHg and right ventricular pressure at 25-30mmHg. Most blood is expelled in the first third of systole causing the proximal arteries to distend to accommodate the fluid bolus. Aortic pressure peaks mid-systole at around 120mmHg and pulmonary artery pressure peaks at around 25mmHg. Ventricular contraction eases and pressure in the ventricles begins to decline in the latter 2/3rds of systole. When left and right ventricular pressures fall below aortic and pulmonary artery pressures respectively, blood flow reverses, causing closure of the aortic and pulmonary valves. Typically around 70-80ml of blood is ejected during ventricular systole (**the stroke volume**) leaving 40-50ml or so in the ventricles at the end of contraction (**the end-systolic volume**). Early ventricular systole corresponds to the ST segment of the ECG, the latter 2/3rds to the T wave.



Cardiac cycle



Cardiac cycle

Phase 5. Ventricular filling.

- Most ventricular filling occurs immediately after the atrio-ventricular valves open then continues gently throughout diastole and before the next atrial contraction. There is usually no ECG deflection during this phase between the T wave and next P wave.



Normal Pressures

- Right Atrium: 5 / 3 mmHg
- Left Atrium: 10 / 8
- Right Ventricle: 28/2
- Left Ventricle 125/6
- Aorta: 120/70

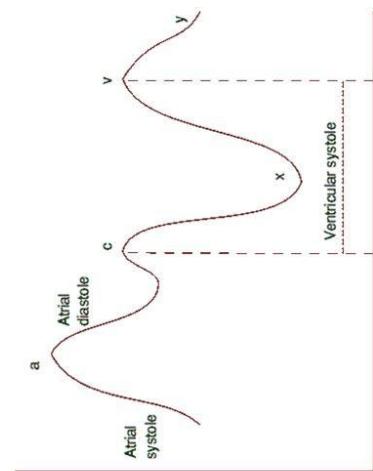
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JVP

- Visible pulsation of internal jugular vein in the neck
- Column of blood arising in right atrium (no valves)
- Height indirectly represents central venous pressure



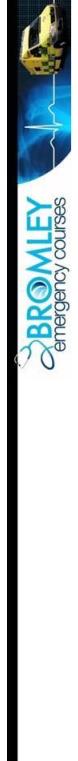
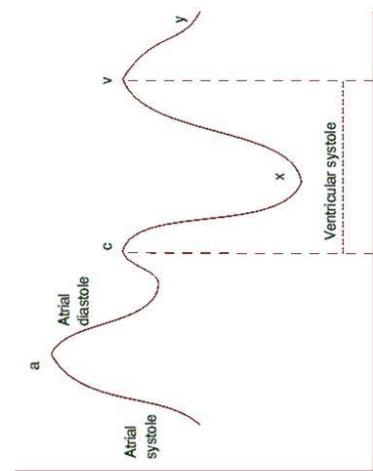
Heart Sounds

- S1- **Mitral and Tricuspid closure**
 - Loudest in the Mitral Region
- S2- **Aortic and Pulmonary Closure**
 - Loudest left sternal border
- S3- **Increased filling pressure. Early diastole.**
 - Most common in hypertension. Can be normal
- S4- **Atrial kick. Late diastole**
 - High atrial pressure. Ventricular hypertrophy
 - Elevated in tricuspid incompetence



JVP

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Heart Sounds

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Splitting S2

- Aortic valve closes before pulmonary
- Inspiration can increase this difference
- Some specific splits:
 - Wide splitting
 - Pulmonary stenosis or RBBB
 - Fixed splitting
 - ASD
 - Paradoxical splitting
 - Aortic stenosis or LBBB



Systolic Murmurs

- MR
 - Blowing.
 - Loudest at Apex
 - radiates to axilla
 - Enhanced by
 - increasing TPR; Squatting
 - Increasing LA return (expiration)
- AS
 - Crescendo-decrescendo
 - ESM
 - Ejection click
 - Radiates to carotids/apex
 - Slow rising pulse
- VSD



Diastolic Murmurs

- Aortic Regurgitation
 - Early diastolic
 - Blowing
 - Wide pulse pressure
 - Patient sitting forwards
 - Full expiration
- Mitral Stenosis
 - Follows opening snap
 - Late diastolic murmur
 - Rheumatic fever



The Control and Maintenance of Mean Arterial Pressure (MAP)



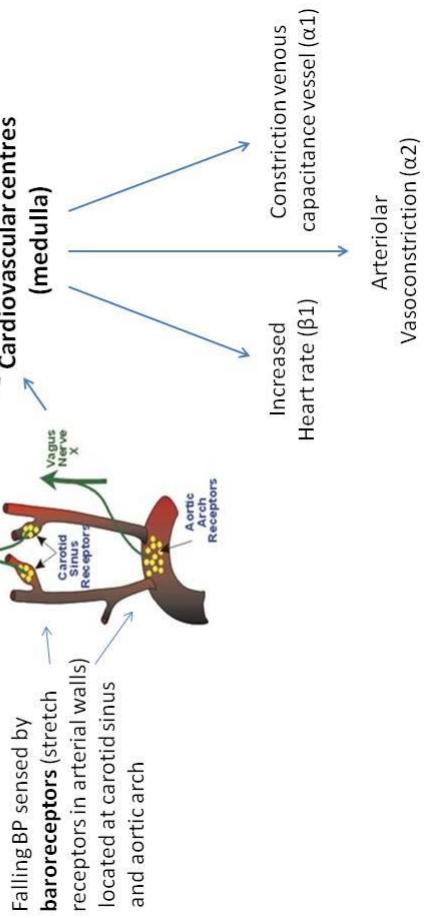


Mean Arterial Pressure

- Normal adult blood pressure 120/80
- Organ perfusion relates more closely to Mean Arterial Pressure (MAP)
- $MAP = CO \times SVR$
- $MAP = \text{diastolic BP} + (1/3 \times (\text{systolic BP} - \text{diastolic BP}))$
- Homeostatic controls maintain MAP between 70 and 110mmHg
- Short term regulation of MAP achieved by rapidly manipulating CO and SVR to keep MAP within normal range (e.g. CV response to orthostasis)
- Background MAP determined by balance of CO, SVR and blood volume.
- Central role : renin-angiotensin-aldosterone system (RAAS) vs atrial natriuretic peptide (ANP)
- Cardiovascular control centres in medulla oblongata



Short term control MAP



Maintenance MAP



That's it folks!



Oxygen delivery to tissues

$$\text{DO}_2 = Q \times \text{CaO}_2$$

$\text{DO}_2 = \text{oxygen delivery}$
(ml O₂/min)

$$\text{CaO}_2 = \text{Hb} \times \text{SpO}_2$$

Oxygen content of blood.

$Q = \text{Cardiac output.}$
Volume blood pumped
out left ventricle per
minute (ml/min)

Objectives

Clinical Pharmacology in ED

- Key Principles

- What Do You Need Know?
- Why Do You Need Know?
- How Do You Need Know?

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Emergency Medicine Consultant
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Objectives

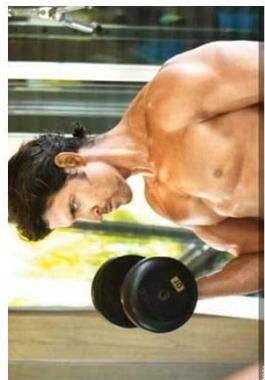
- Some Keys concepts
- Some high yield topics
- Part B: Some questions

Top 10 Pharmacological Principles

- Bioavailability
- Volume of Distribution (V_d)
- Loading Dose
- Metabolism
- Elimination
- Clearance
- Half-Life
- Dose response curves
- Therapeutic Window
- Agonist & Antagonists

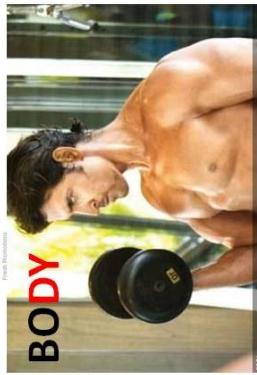
Definitions

- Pharmacokinetics
 - Absorption
 - Distribution
 - Metabolism
 - Excretion



Definitions

- Pharmacodynamic
 - Drug-receptor interaction
 - Dose-Response
 - Potency
 - Therapeutic Index



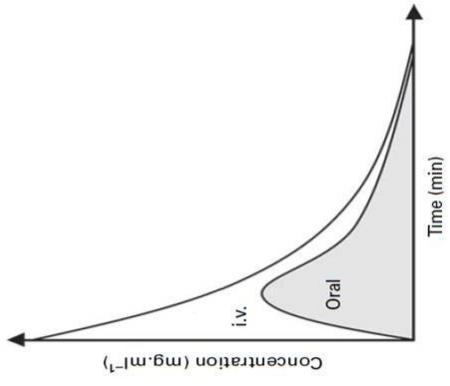
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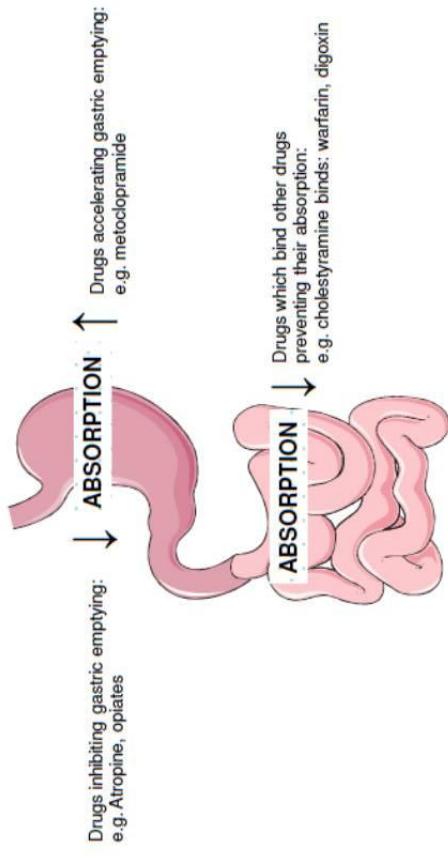
Bioavailability

- Defⁿ: The amount of drug that reaches the systemic circulation
- Unity is defined as intravenous route

$$\text{Bioavailability} = \frac{AUC[\text{plasma}] - \text{route}}{AUC[\text{plasma}] - i.v.}$$



Changes in drug absorption



Water / Lipid Solubility

- Lipid soluble molecules are better absorbed
- Unionized molecules are more lipid soluble
 - Faster absorption



U



I

Volume of Distribution

$$V_d = \frac{\text{Drug(mg)}}{[\text{Drug}]_{\text{plasma}} (\text{mg/L})}$$

Top 10 Pharmacological Principles

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- Apparent Volume
- Low V_d (e.g. warfarin, gentamicin)
- Medium V_d (diazepam)
- High V_d (e.g. Digoxin, Chloroquine)

Volume of Distribution

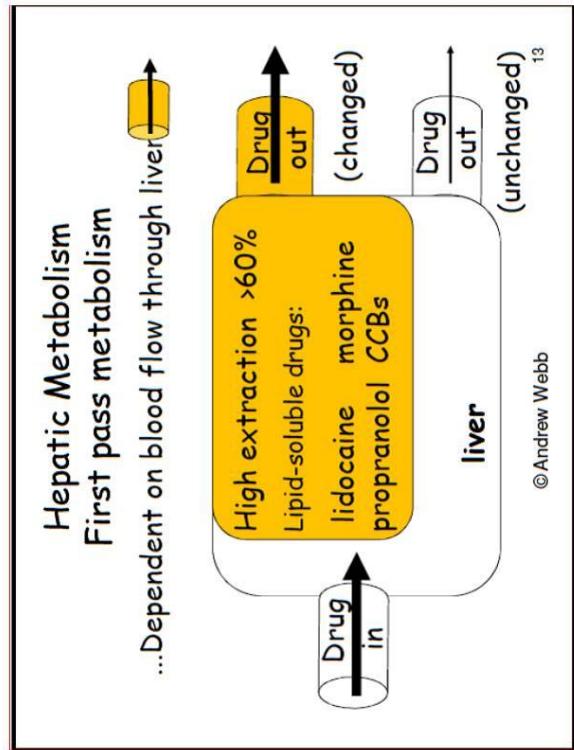
- For most patients its related to the patients weight
- Is the drug lipid soluble?
 - Chloroquine
- Can be used to calculate the loading dose:
 - $\text{Loading dose} = [\text{Drug}]_{\text{plasma}} \times V_d$

Top 10 Pharmacological Principles

- Bioavailability
- Volume of Distribution (V_d)
- Loading Dose
- **Metabolism**
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Metabolism

- Phase I:
 - Oxidation (cytochrome P450)
 - Reduction
 - Deamination
 - Hydrolysis
- Makes the drug more water soluble or more reactive
- Enzymes mostly produced in the liver



Metabolism

- Phase II: Involves conjugation
 - Acetylation
 - Sulfation
 - Glucuronidation
 - Addition of many other groups
- They make products less lipid-soluble
 - Less likely to be reabsorbed in the urine

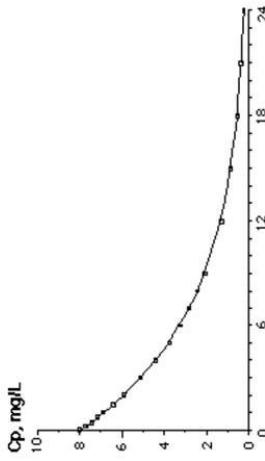
Cytochrome P450 (CYP)

- CYP are responsible for 75% of drug metabolism
- Mostly found in the liver
- CYP3A4- metabolises most drugs
- Drugs can be either **inhibitors** or **inducers** of these enzymes
- Pharmacogenetics:
 - CYP2D6 polymorphic in 6% Caucasians

Top 10 Pharmacological Principles

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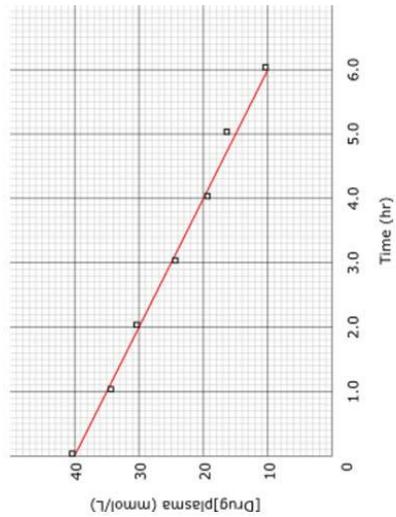
First Order Kinetics



- Greater concentration the greater the amount of drug eliminated

Zero Order Kinetics

- Enzymes are saturated
- Constant amount of drug is eliminated per unit time regardless of concentration
- Alcohol, aspirin, and phenytoin



Top 10 Pharmacological Principles

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- Clearance **Red Box**
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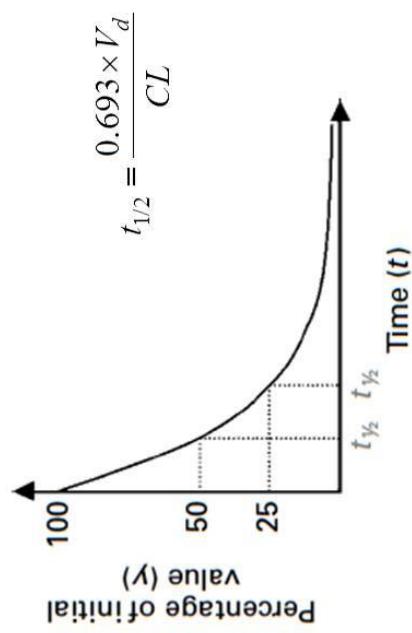
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Clearance

- Clearance = Rate of elimination / $[Drug]_{\text{plasma}}$
- Clearance depends on the drug (1/2 life) and the condition of the organ of elimination
- First order: clearance is constant
- Clearance = $k \cdot V_d$

Half Life



Steady State

- For a continuous infusion:
 - Rate of infusion = Rate of elimination
 - Usually 4-5 $t_{1/2}$
- A knowledge of half life can dictate dosing regime

Definitions

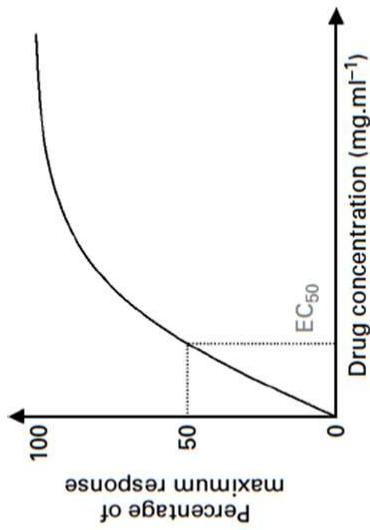
- Efficacy: Is a measure of the magnitude of effect
- Potency: The amount of drug needed to produce a desired affect

Pharmacodynamics

Top 10 Pharmacological Principles

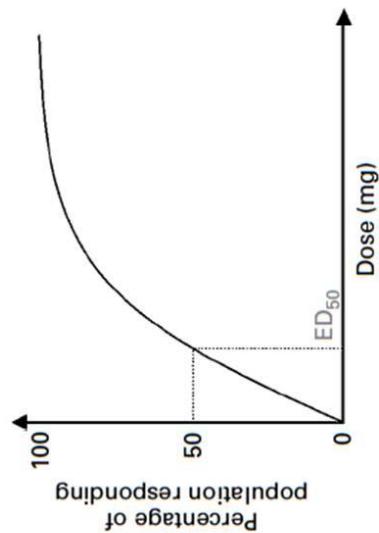
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Dose Response Curve



EC_{50} is the concentration at which 50% of the maximum effect occurs

Quantal Dose Response Curve



ED_{50} is the dose required to cause 50% of the population

Top 10 Pharmacological Principles

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Therapeutic Index

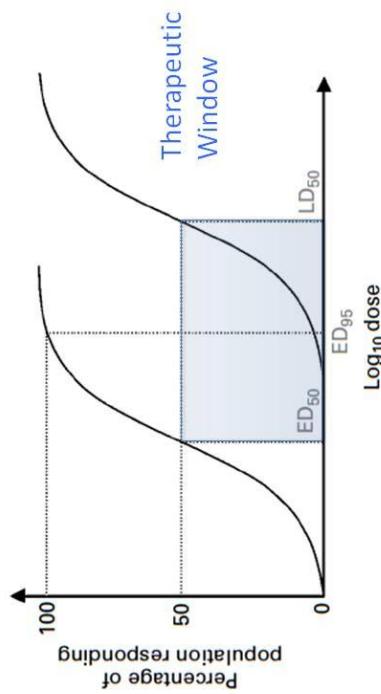
The therapeutic index
(also known as **therapeutic ratio**)

$$\text{Therapeutic ratio} = \frac{\text{LD}_{50}}{\text{ED}_{50}}$$

- lethal dose of a drug for 50% of the population (LD_{50})
- minimum effective dose for 50% of the population (ED_{50})
- The therapeutic index for diazepam is somewhat forgiving, about = 100.
- Other drugs, however are much less so, such as Digoxin, which has an index of 2 or 3.

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Therapeutic Window



LD_{50} is the dose required to cause 50% of the population

Drugs with narrow therapeutic range

Renally excreted:

- digoxin*
- gentamicin*
- vancomycin*
- lithium*
- (metformin)
- Reduce dose if:
 - Cr >150 umol/l
 - GFR <50ml/ min
- *Use therapeutic drug monitoring

Hepatically metabolised:

- Phenytoin*
- ciclosporin*

Top 10 Pharmacological Principles

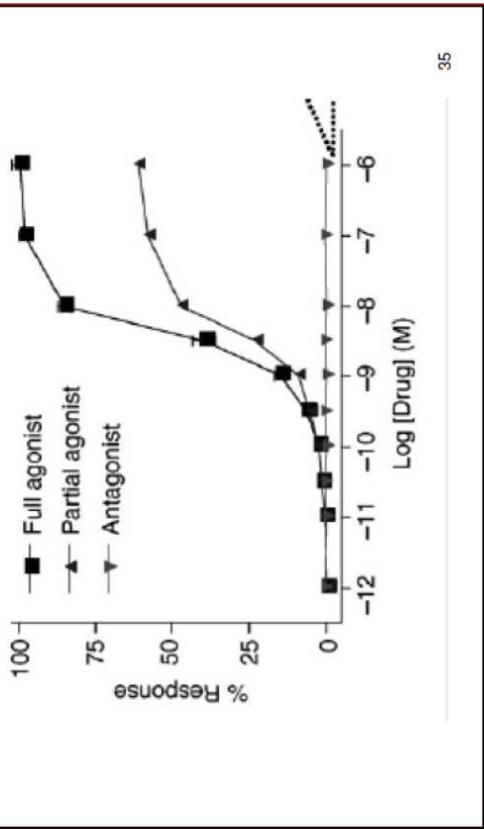
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- **Agonist & Antagonists**

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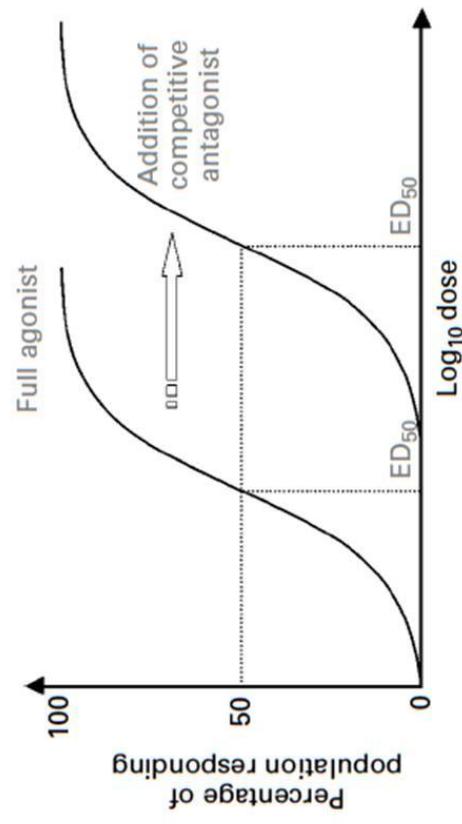
Definitions

- Agonist: A drug that has significant receptor affinity and once bound produces an effect
 - Full agonist: Maximal effect when bound
 - Partial agonist: Sub maximal effect
- Antagonist: Has significant affinity but **NO** response

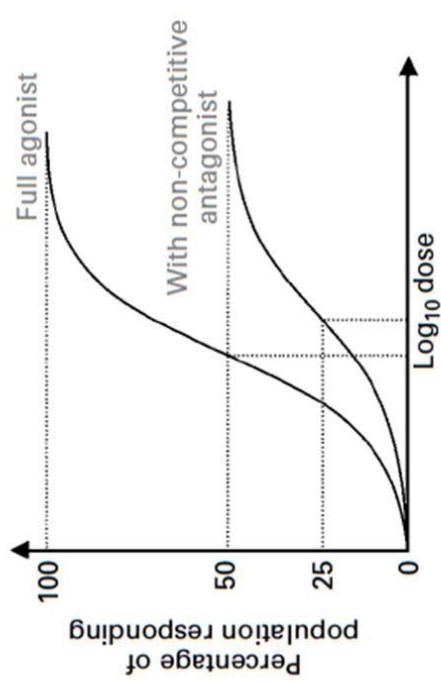
Agonists/Antagonists



Competitive Antagonist



Non Competitive Antagonist





Objectives

- High Yield Topics
- Questions

Clinical Pharmacology in ED

- Questions and High Yield Topics

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Emergency Medicine Consultant
Princess Royal University Hospital

High Yield Topics

- Drugs affecting the Autonomic system
 - Various receptors
 - Bedside manifestations of the drugs
- Anaesthetic and sedative agents
- Drug
- Adverse Reactions
 - System based
 - CYP
- Drug toxicity
- Antibiotics

Haematological Reactions

- **Agranulocytosis:** Clozapine, Carbamazepine, colchicine, methimazole
- **Aplastic anaemia:** Chloramphenicol, NSAIDs, propylthiouracil, methimazole
- **Megaloblastic Anaemia:** Phenytoin, Methotrexate, Sulfa drugs
- **Myelosuppression:** Chemotherapy, azathioprine, leflunomide,

Others

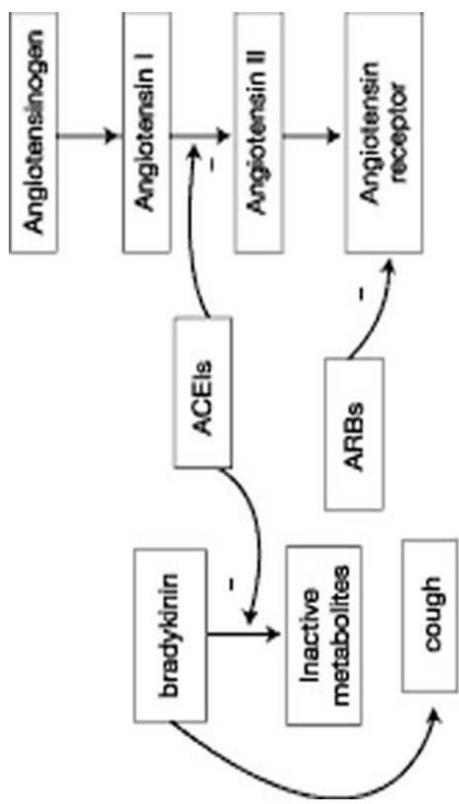
• Haemolysis in G6PD Deficiency:

- Isoniazid, sulfonamides, primaquine, aspirin, ibuprofen, Nitrofurantoin

• OCP

- Increase tendency towards thrombosis

ACE Inhibitors



Intravenous induction agents: physiological effects

	Thiopental	Methohexitol	Propofol	Ketamine	Benzodiazepine
Blood pressure	↓	↓	↓↓	↑	↔
Cardiac output	↓	↓	↓↓	↑	↔
Heart rate	↑	↑	↑↑	↑	↔
Systemic vascular resistance	↓↓	↓↓	↓↓	↔	↔
Respiratory rate	↓	↓	↓	↓	↓
Intracranial pressure	→	→	→	↑	↔
Intraocular pressure	↑	↑	↑	↑	↔
Pain on injection	No	Yes	Yes	No	Yes
Nausea/vomiting	No	No	No	Yes	Yes
Miscellaneous	Intra-arterial injection → crystallization	↓ Fit threshold	? Toxic in children (metabolic acidosis and bradycardia)	↑ Salivation 'dissociative anesthesia'	Adrenal suppression

Liver Enzyme Inhibitors

• AODEVICES

- Allopurinol and Amiodarone
- Omeprazole
- Disulfiram
- Erythromycin
- Valproate
- Isoniazid
- Cimetidine (and Ciprofloxacin)
- Acute Ethanol intoxication
- Sulphonamide

Class	Mechanism	Drugs	PR- Interval	QRS Duration	QT Interval
1A	Na ⁺ -Channel Blocker (Atrial and Vent)	Quinidine Procainamide	↑ or ↓	↑↑	↑↑
1B	Na ⁺ -Channel Blocker (Ischaemic Tissue)	Lidocaine Phenytoin	↓		
1C	Na ⁺ -Channel Blocker (Atrial only)	Flecainide		↑↑	
2	Beta Blockade (Slows AV conduction)	Atenolol Metoprolol	↑↑		
3	K ⁺ Channel Blockade	Amiodarone Sotalol	↓	↑↑	↑↑↑
4	Ca ²⁺ -Channel Blockade	Diltiazem Verapamil	↑↑↑		

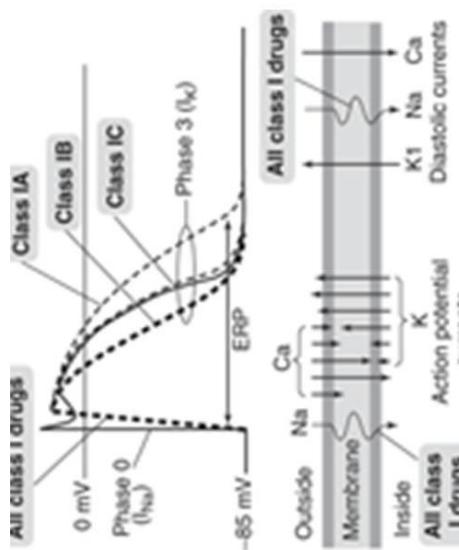
Enzyme Inducers

- PCBRAS

- Phenytoin
- Carbamazepine
- Barbiturates
- Rifampacin
- Alcohol Excess
- Sulphonylurea

Antipsychotics

- Typical: Haloperidol, Chlorpromazine
 - Adverse Reaction:
 - Extrapyramidal
 - Anticholinergic
 - Histaminic
 - Neuroleptic Malignant syndrome
- Atypical: Clozapine, Quetiapine, Olanzapine
 - Adverse Reaction:
 - As above but much less likely
 - Sexual dysfunction



Overdoses

Know your fluids

Paracetamol overdose
 Tricyclic antidepressant overdose
 Theophylline toxicity
 Carbon monoxide poisoning
 Quinidine and quinine toxicity
 Iron poisoning
 Salicylate overdose
 Ethylene glycol poisoning
 Haemodialysis for overdose or poisoning

Intravenous fluids: crystalloids

	Na ⁺ (mmol.l ⁻¹)	K ⁺ (mmol.l ⁻¹)	Ca ²⁺ (mmol.l ⁻¹)	Cl ⁻ (mmol.l ⁻¹)	HCO ₃ ⁻ (mmol.l ⁻¹)	Osm (mmol.l ⁻¹)	pH	Glucose (g.l ⁻¹)
0.9% Saline	154	0	0	154	0	300	5	0
5% Dextrose	0	0	0	0	0	280	4	50
10% Dextrose	0	0	0	0	0	560	4	100
4% Dextrose, 0.18% saline	31	0	0	31	0	255	4.5	40
Hartmann's solution	131	5	2	111	29	278	6	0
8.4% NaHCO ₃	1000	0	0	0	1000	2000	8	0

Intravenous fluids: colloids

	Composition	M _w (kDa)	Na ⁺ (mmol.l ⁻¹)	K ⁺ (mmol.l ⁻¹)	Ca ²⁺ (mmol.l ⁻¹)	Mg ²⁺ (mmol.l ⁻¹)	Cl ⁻ (mmol.l ⁻¹)	Osm (mmol.l ⁻¹)	pH
Gelofusine	Succinylated gelatin	30-35	154	0.4	0.4	0.4	125	279	7.4
Haemaccel	Polygelines	30-35	145	5.1	6.25	0	145	301	7.3
Hydroxyethyl starch (HES)	Esterified amylopectin	450	154	0	0	0	154		
Dextran 70	Polysaccharides in 5% dextrose	70	0	0	0	0	0	287	3.5-7
HES 4.5%	Fractionation of plasma	69	100-160	<2	0	0	100-160	270-300	6.4-7.4
HES 20%		69	50-120	<10	0	0	<40	135-138	6.4-7.4

With traumatic injury to the brachial plexus

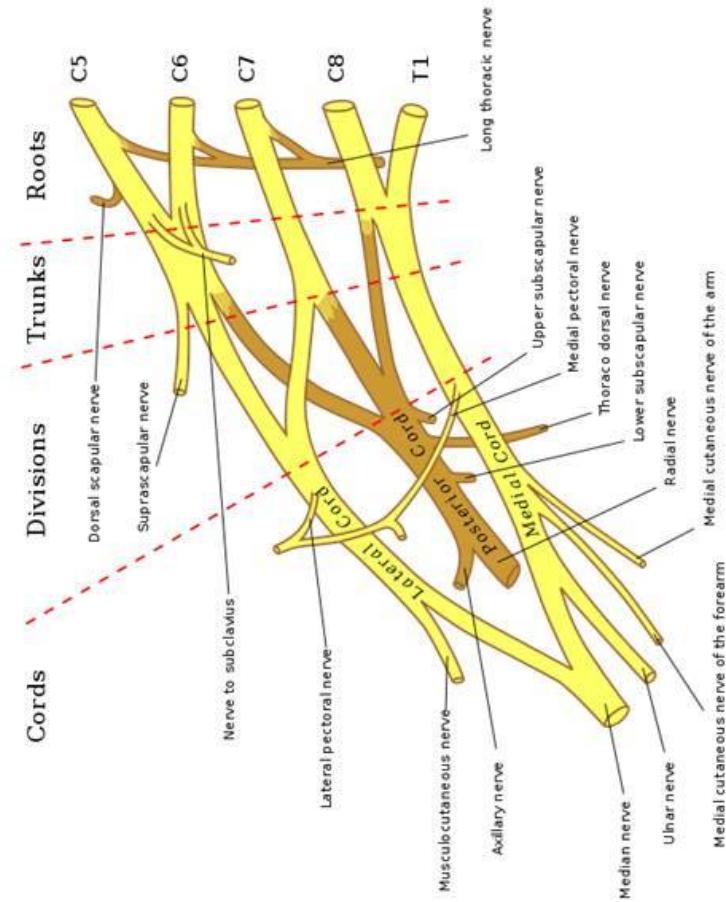
- a. Horner's syndrome may also be seen
(T)
- a. The prognosis for pre-ganglionic lesions is generally favourable
(F)
- a. Upper brachial plexus injury gives weakness of the elbow flexors and wrist extensors
(T)
- d. lower brachial plexus injuries commonly arise from traction on the abducted arm during a difficult childbirth
(T)

Upper limb and Head & Neck

Dr Chet Trivedy

BDS FDS.RCS (Eng) MBBS PhD MCEM FRSH

The brachial plexus (Pin 5363)



Posterior cord branches (ULTRA)

- upper subscapular
- Lower subscapular
- Thoracodorsal
- **Radial**
- **Axillary**

Lateral Cord Branches (Lucy Loves Me)

- Lateral pectoral
- **Lateral root of the median nerve**
- Musculocutaneous

Medial Cord Branches (Medical Men Must Use Morphine)

- Medial pectoral,
- Medial cutaneous nerve of arm
- Medial cutaneous nerve of forearm
- **Ulnar**
- **Medial root of the median nerve**

Brachial Plexus Injuries

Upper brachial plexus injury (TEAR)

- Traumatic birth
- Erbs palsy
- Arm extended with wrist drop
- Root of brachial plexus

Lower brachial plexus injury (THICK)

- Traumatic birth
- Horner's syndrome
- Inferior (lower) brachial plexus injury
- Claw hand
- Klumpke's palsy

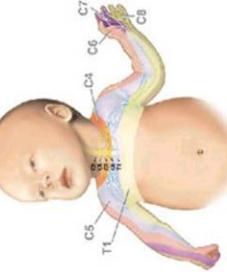
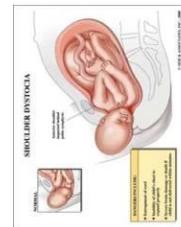
Erbs palsy

Upper brachial plexus injury (TEAR)

- Traumatic birth
- Erbs palsy
- Arm extended with wrist drop
- Root of brachial plexus

Lower brachial plexus injury (THICK)

- Traumatic birth
- Horner's syndrome
- Inferior (lower) brachial plexus injury
- Claw hand
- Klumpke's palsy



Klumpkes Palsy



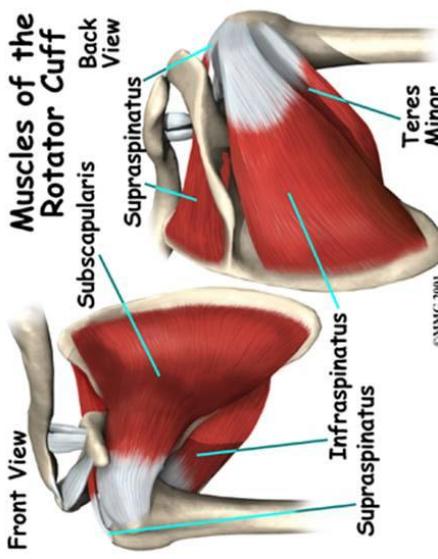
The following statements about the shoulder are true

- a. The muscles of the rotator cuff are supraspinatus, infraspinatus, teres minor and teres major **(F)**
- b. The shoulder tip is usually dermatome C3 **(F)**
- c. Subscapularis is an external rotator of the humerus **(F)**
- d. The axillary nerve innervates deltoid muscle **(T)**



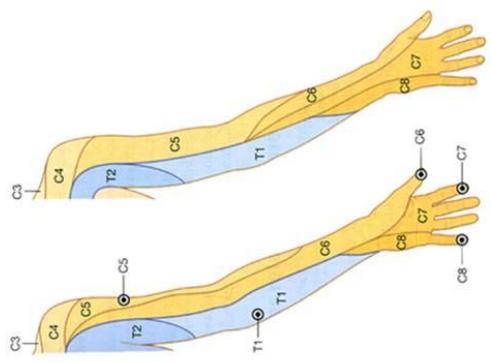
Rotator Cuff

Rotator Cuff



Muscle	Nerve supply	Action
Supraspinatus	Suprascapular nerve	C5
Infraspinatus	Suprascapular nerve	C5 C6
Teres minor	Axillary nerve	C5
Subscapularis	Subscapular nerve	C5 C6

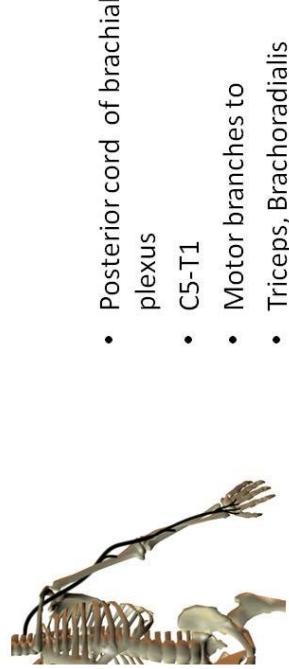
Dermatome Innervation Upper Limb



Radial nerve function maybe assessed by

- a. Looking for biceps wasting
(F)
- b. Asking the patient to supinate the forearm against resistance
(T)
- c. Asking the patient to extend the fingers from the clenched fist position
(T)
- d. Testing for light touch sensation over the thenar eminence
(F)

The Radial Nerve



- Posterior cord of brachial plexus
- C5-T1
- Motor branches to Triceps, Brachioradialis
- Extensor carpi radialis longus and brevis
- Supinator
- Abductor pollicis longus
- Extensors of wrist fingers

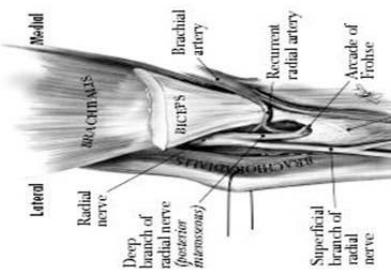


Radial Nerve Injuries (1)

Causes

- Different levels of injury
- Axilla (use of crutches and Saturday night palsy)
- Upper arm (injections/fracture of shaft of humerus)
- Elbow nerve entrapment
- Wrist nerve entrapment

Arcade of Frohse

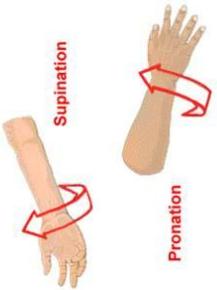


Radial Nerve Injuries (2)

Site of radial nerve lesion	Features
Axilla	Wrist drop Lower brachial plexus involvement may present with median and ulnar nerve injury
Upper arm	Triceps supplied above spiral groove Brachioradialis Extensor carpi radialis longus and brevis supplied below the groove
Elbow	Pain on supination Tenderness over radial tunnel Pain on finger extension
Wrist	Finger drop but no wrist drop

Radial Nerve Testing

Muscle	Action
Triceps (C78)	Extend elbow against resistance
Brachioradialis (C56)	Flex elbow with forearm between supination and pronation
Supinator (C56)	Resist pronation with arm by side
Extensor Carpi Radialis Longus (C78)	Extend wrist to radial side with fingers extended
Extensor digitorum (C78)	Extend fingers at MCP

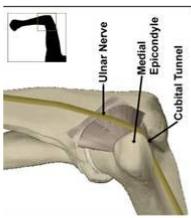


Ulnar nerve severance at the elbow will cause

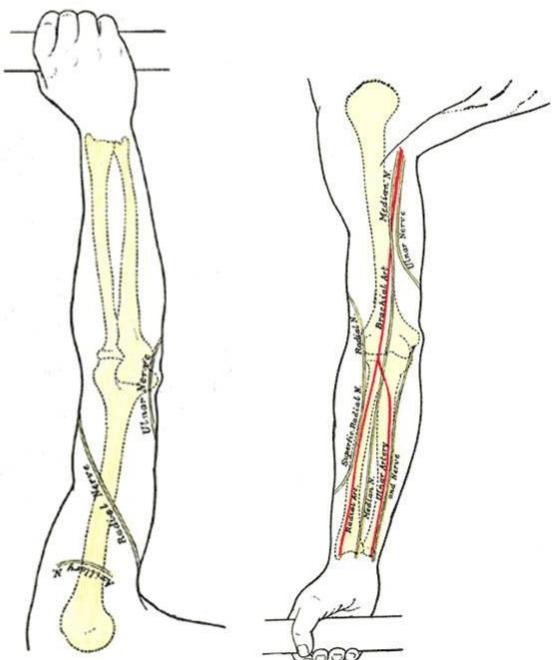
- a. Ulnar deviation of the wrist in flexion
(F)
- b. Paralysis of the lateral half of flexor digitorum profundus
(F)
- c. Wasting of the hypothenar eminence
(T)
- d. Claw hand
(T)

Ulnar Nerve

- C8-T1 which forms the medial cord of the brachial plexus
- Ascends down the posteromedial aspect of the humerus
- Commonly entrapped at
 - Elbow (Cubital tunnel)
 - At the wrist in Guyon's canal
 - In the hand due to pressure against pisiform and hamate (cyclists/ pneumatic drill workers)



Course of the Ulnar Nerve



Motor Innervation

- Flexor Carpi ulnaris
- Medial half of the flexor digitorum profundus
- Hypothenar eminence
- Small muscles of the hand except lateral two lumbricals, opponens pollicis, abductor pollicis brevis and flexor pollicis brevis

Ulnar Nerve

Site	Features	Test
Elbow	Wasting of flexor carpiulnaris Wasting of small muscles of hand except thenar eminence and 1 st two lumbricals Clawing of ring and little fingers	Deviation of hand to radial side as wrist is flexed Clawing of ring and little fingers Failure to abduct or adduct fingers Fronten's sign
Below elbow		Paresthesia over 5 th and ulnar half of 4 th finger and ulnar edge of palm
Wrist	Cubital tunnel clawing more prominent as FDP is preserved. Wrist flexion unaffected as flexor carpiulnaris is spared	
Hand	No sensory loss and sparing of the dorsal cutaneous branch of the ulnar nerve Hypothenar eminence spared	Clawing more prominent It is due to Hyperextension at the MCP and flexion of IP joint



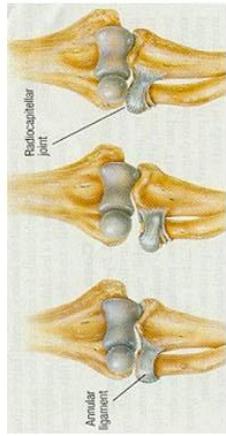
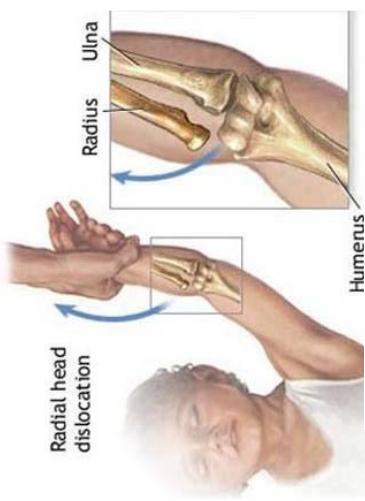
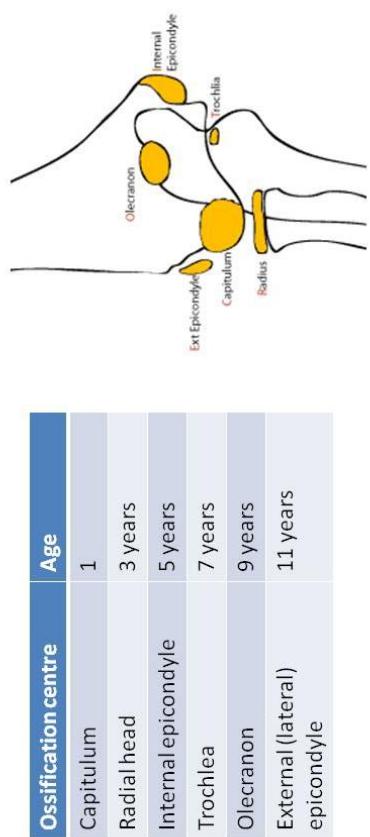
Supracondylar Fracture

- Extension fracture (95%) FOOSH /hyperextension mechanism
- Flexion fractures less common (5%) posterior blow to a flexed elbow
- Gartland I-III (Type I undisplaced and managed with cast immobilisation
- Gartland II-III increasing amount of displacement which may require ORIF
- Aware of significant complications secondary to neurovascular deficit (Volkmann's, compartment syndrome, nerve damage)

The following are true of elbow injuries in children

- All supracondylar fractures require surgical fixation (**F**)
- Ossification of lateral epicondyle occurs before the medial epicondyle (**F**)
- The brachial artery is at risk in elbow dislocation (**T**)
- 'pulled elbow' in the child is a term given to subluxation of the radial head from the annular ligament (**T**)

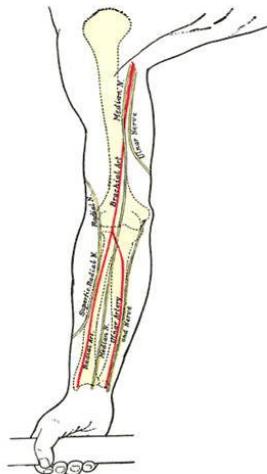
Pulled elbow



Median nerve injury at the wrist causes:

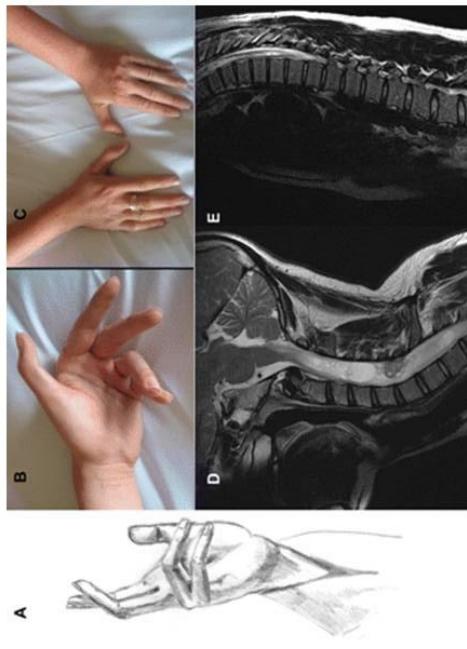
- a. Loss finger flexion
(F)
- a. Loss of sweating over the index finger
(T)
- c. Loss of sensation in the radial three digits
(T)
- d. Loss of thumb adduction
(F)

Median Nerve



- C5-T1 from medial and lateral cords of the brachial plexus
- Only nerve that passes through carpal tunnel
- No motor or sensory supply in the arm sympathetic fibers to the brachial artery
- Hand of Benediction due to loss of finger flexion of 2/3 digits secondary to median nerve section at elbow or above

Benediction Sign



Median Nerve Motor Innervation

Arm		Autonomic
Forearm (superficial)	Pronator teres Flexor Carpi radialis Palmaris longus	
Forearm (Intermediate)	Flexor digitorum superficialis	
Forearm (deep)	Ant osseous nerve supplies Lateral half of flexor digitorum profundus Flexor pollicis longus Pronator quadratus	
Hand	LOAF Lumbricals 1&2 and thenar eminence (opponens pollicis, abductor pollicis brevis, flexor pollicis brevis)	

Median Nerve Lesions

Injury level	Clinical features
Above elbow	Reduced pronation and flexion of fingers
Elbow	Pronator teres syndrome
Forearm	Anterior osseous syndrome
Wrist	Carpal tunnel syndrome Loss of pincer movement and OK sign Median palmar sensory loss 3 1/2 fingers and dorsal finger tips Simian hand



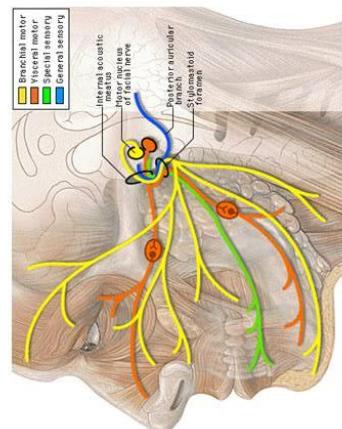
Regarding the facial nerve:

- a. It emerges through the stylomastoid foramen (F)
- a. It lies deep to the parotid gland (T)
- c. It has bilateral cortical innervation (T)
- d. Infranuclear lesions may cause reduced hearing due to paralysis of stapedius (F)

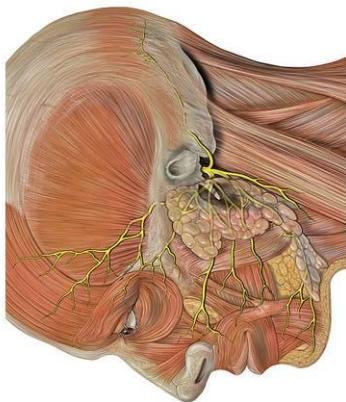
Facial Nerve

Facial nerve (II)

- VII Cranial nerve
- Muscles of facial expression (TZBMC)
- Sensory behind ear
- Taste via chorda tympani
- Parasympathetic fibres to lacrimal and salivary glands



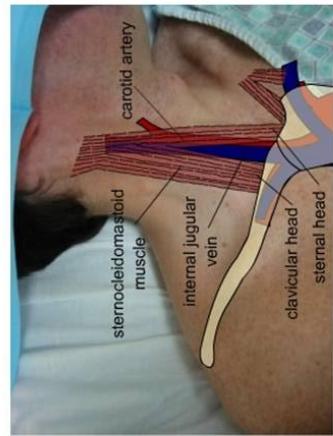
- Within the body of the parotid gland
- Bilateral cortical innervation which explains UMN lesions have frontal sparing
- Stapedius action is to dampen hearing if affected hyperacusis



Regarding the anatomy of the internal jugular vein the following are correct

- a. It is a continuation of the transverse sinus (**F**)
- b. It joins the external carotid vein (**F**)
- c. Runs medial to the internal carotid artery (**F**)
- d. Drains the floor of the mouth via the lingual vein (**T**)

Internal Jugular Vein

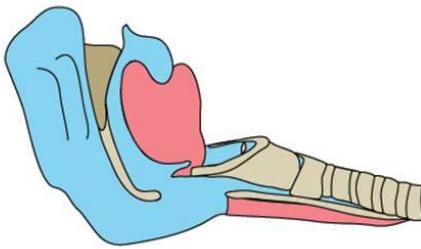


- Formed by union of the inferior petrosal and sigmoid sinus
- Leaves through jugular foramen
- Drains facial, lingual and retromandibular veins
- Lateral to internal and common carotid
- Drains into subclavian vein

Adult and Paediatric Airway

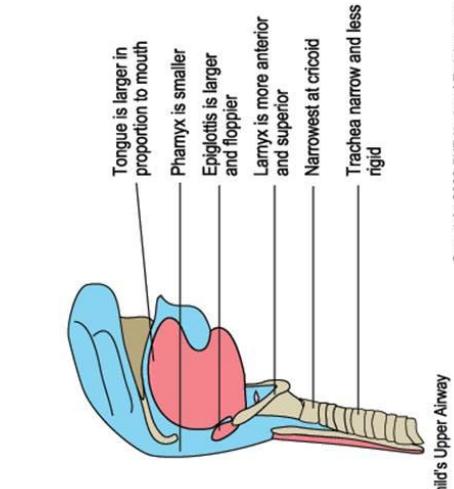
The paediatric airway differs from the adult in that:

- a. The narrowest part is at the level of the glottis (F)
- b. The epiglottis is more floppy (T)
- c. The tongue is relatively smaller (F)
- d. There is a different intubation technique (T)



Adult's Upper Airway

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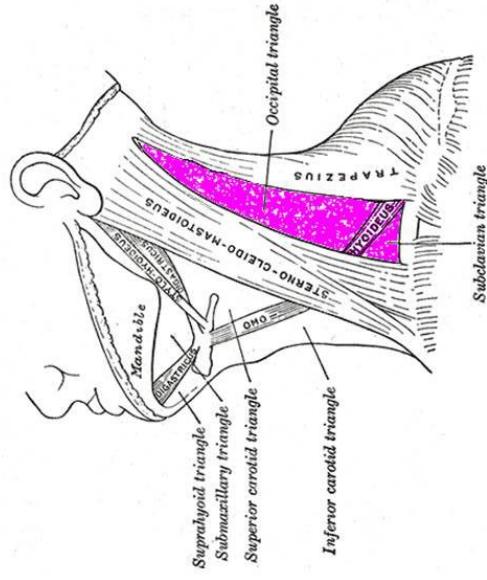
Child's Upper Airway

For children head position is neutral and sniffing the morning air is not helpful to bag valve or visualise the glottis

The posterior triangle of the neck

- a. Contains the accessory nerve (T)
- b. Contains branches of the cervical plexus (T)
- c. Contains the internal jugular vein (F)
- d. Has the anterior margin of sternocleidomastoid muscle as its posterior border (F)

Posterior Triangle



Contents of the Posterior Triangle

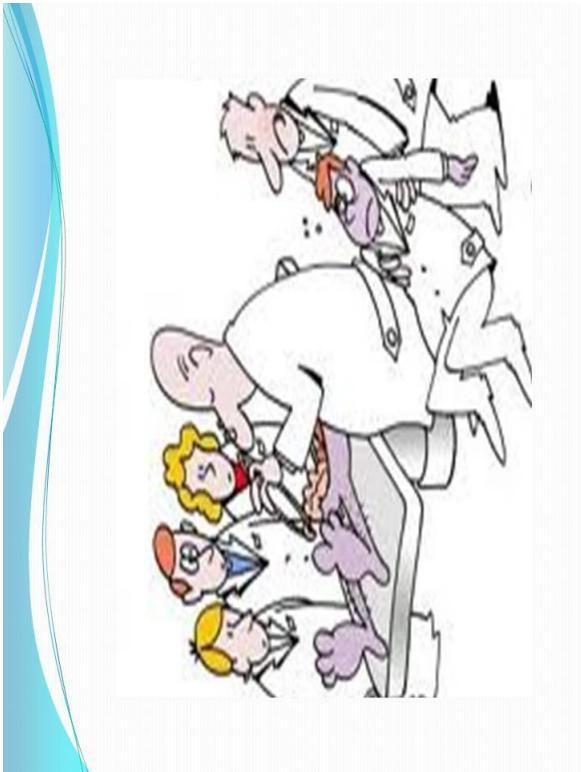
Questions

Content of Posterior Triangle of the Neck	
Nerves	Spinal accessory Cervical plexus Roots of brachial plexus Phrenic nerve
Vessels	3 rd Part of subclavian artery Terminal part of external jugular vein Transverse cervical artery Suprascapular artery
Muscles	Anterior /Middle /Post Scalene muscles Omohyoid Levator scapulae Spleniulus
Lymph nodes	Occipital SuprACLavicular



- If you were to pray to a living god of anatomyhis name would be

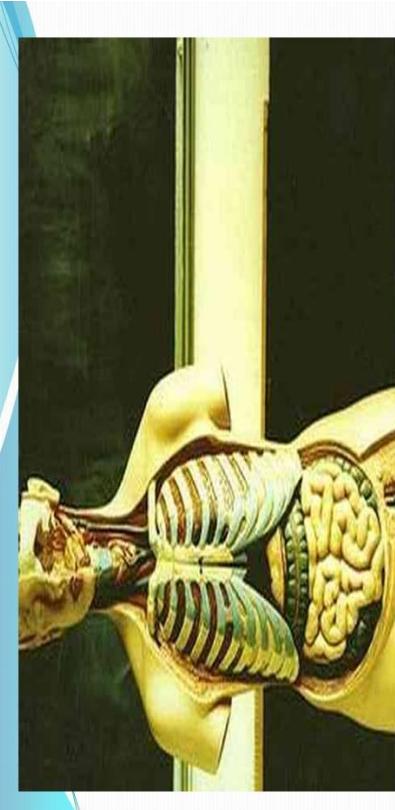
Prof Harold Ellis



Lower limb and torso :

MCQs & Applied Anatomy

TT JAIGANESH
MS; DNB; DCH; FRCS(Surg); FRCS(A&E); FCEM
26 & 27 April 2014
GAMET, CHENNAI



Clinical Anatomy

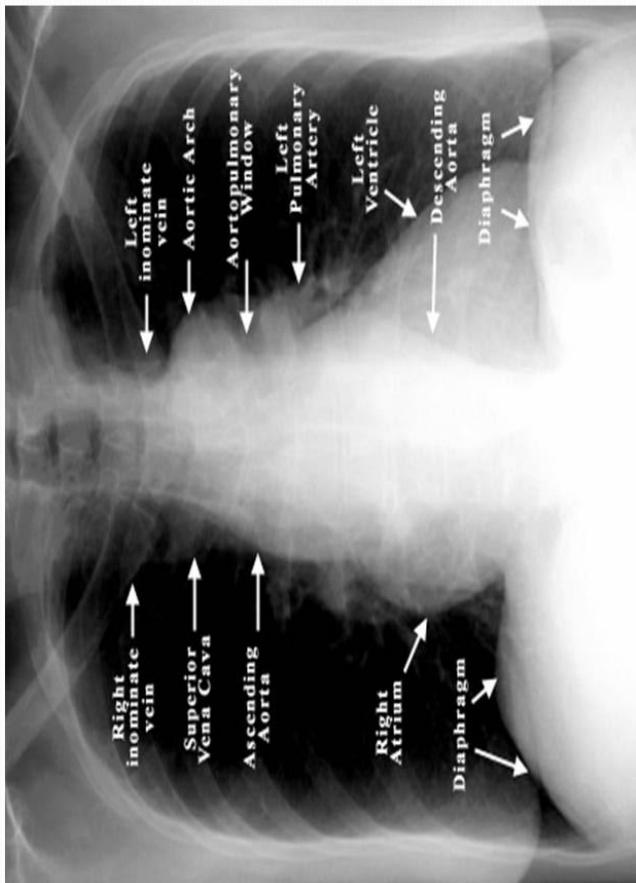
Applied anatomy for students and junior doctors

Harold Ellis

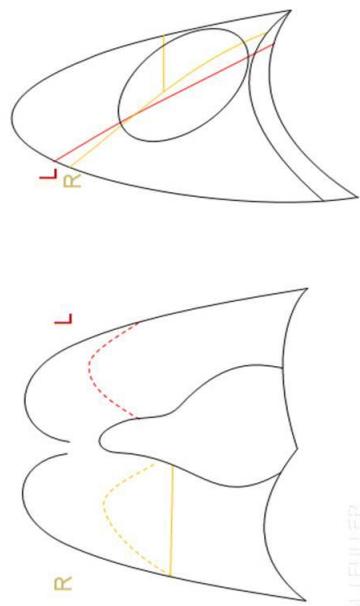
Blackwell Publishing

The following are true of the PA chest X-ray in a normal adult

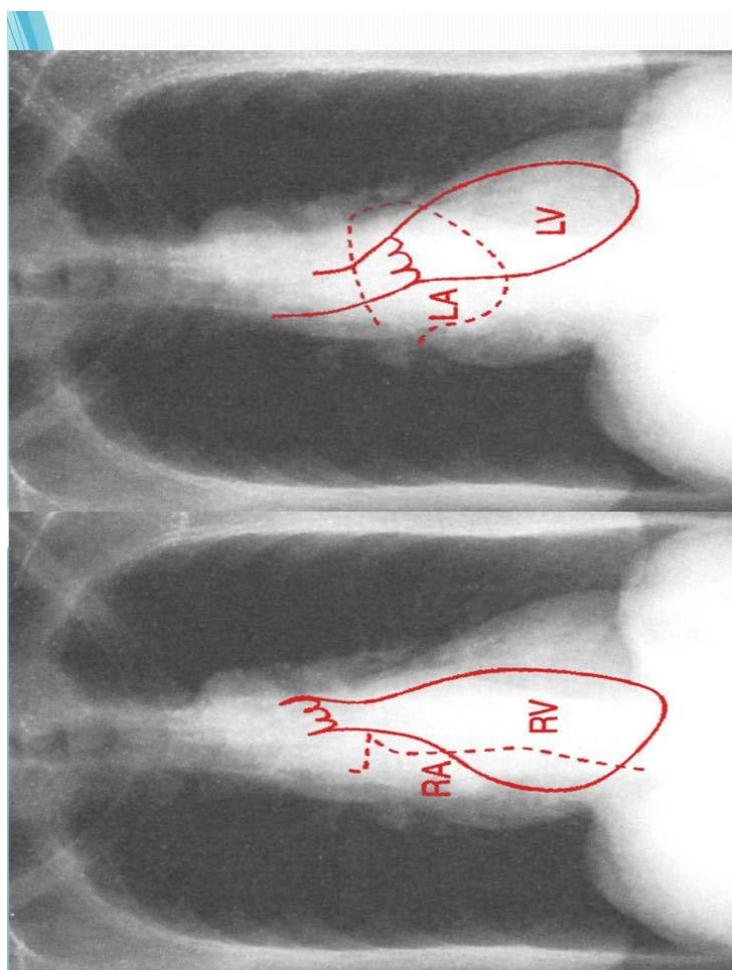
- a. the horizontal fissure runs from the centre of the right hilum to the 6th rib at the axillary line (T)
- b. the right ventricle forms the majority right heart border (F)
- c. the right middle lobe sits adjacent to the right heart border (T)
- d. the left diaphragm is usually higher than the right (F)



The Fissures of the Lung



M.J. FULLER



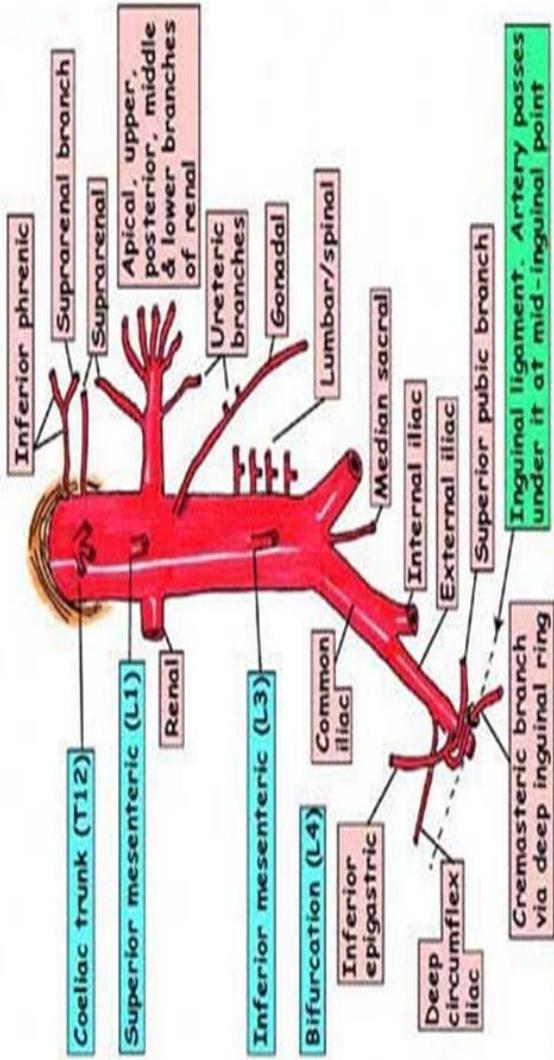
The following are true of the abdominal aorta

- a. it gives off the testicular artery in males
(T)
- b. its maximal normal diameter is 4cm
(F)
- c. it bifurcates into the common iliac arteries at the level of L₄
(T)
- d. it sits in front of the lumbar spine separated from it by only the anterior longitudinal ligament
(T)

Right Middle Lobe



ABDOMINAL AORTA AND RIGHT EXTERNAL ILIAC ARTERY



Major Branches of Celiac Trunk, Superior Mesenteric and Inferior Mesenteric Arteries

Celiac Trunk

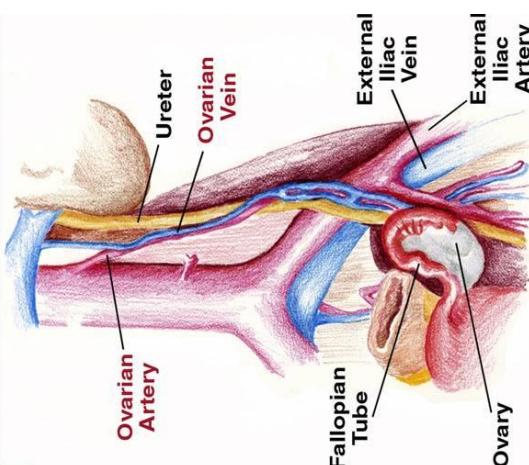
- Splenic artery
 - left gastro-omental
 - dorsal pancreatic
 - greater pancreatic
 - short gastrics
- Common hepatic artery
 - Gastro-duodenal artery
 - gives rise to anterior and posterior/superior pancreaticoduodenal arteries
 - right gastro-omental artery
 - Hepatic proper
 - right and left hepatic arteries

Branches of SMA

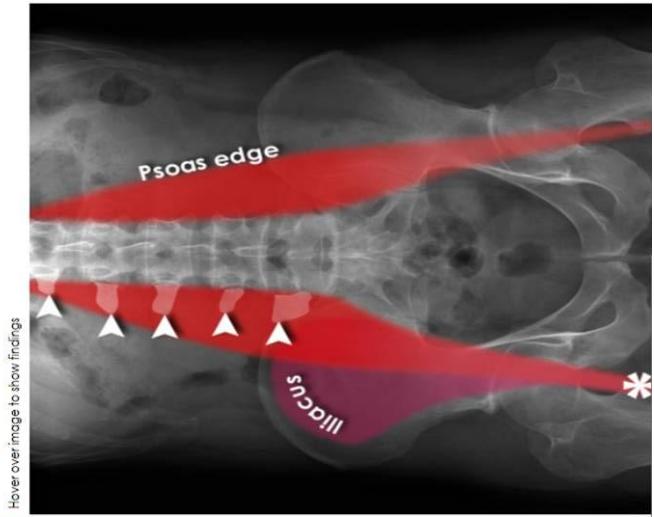
- Intestinal arteries (arcades—vasa recta—straight arteries)
- Ileocolic artery
 - appendicular artery
 - Right Colic artery
 - Middle Colic artery
- Inferior pancreaticoduodenal artery
- Braches of IMA
 - Left Colic artery
 - anastomoses with middle colic via marginal artery
 - Sigmoidal artery branches
 - Superior Rectal arteries
 - Middle Rectal (from internal iliac artery)
 - Inferior Rectal (from internal pudendal artery)

Gonadal Vessel

- Testicular arteries arise from ABD aorta just inferior to renal arteries...pass retroperitoneally to reach deep inguinal rings
- Testicular veins emerge from testis to form pampiniform plexus.
- L vein empties in L renal vein, R vein in IVC.



Psoas edges on abdominal X-ray



Hover over image to show findings

Regarding a patient with retroperitoneal haemorrhage

- a. flank bruising (Grey Turner's sign) occurs (T)
- b. splenic laceration is a cause (F)
- c. loss of psoas markings on the plain abdominal film is a sign (T)
- d. correctly performed FAST ultrasonography is useful in diagnosis (F)

Regarding the anatomical relationships of the adult ureters

- a. on X-ray, they lie just lateral to tips of transverse processes of lumbar vertebra (T)
- b. the are retroperitoneal for most of their course (T)
- c. the vesico-ureteric junction is located on the anteromedial aspect of the urinary bladder (F)
- d. the ureters are at their widest diameter as they cross the common iliac arteries (F)

Psoas edges on abdominal X-ray

The psoas muscles (red) arise from the transverse processes of the lumbar vertebrae (arrowheads) and combine with the iliacus muscles. Together these powerful muscles form the iliopsoas tendon, which attaches to the lesser trochanter of the femur (*). The iliopsoas muscles are the flexors of the hip.

An abdominal X-ray often demonstrates the lateral edge of the psoas muscles as a near straight line. The iliacus muscles are not visible, as they lie over the iliac bones of the pelvis.

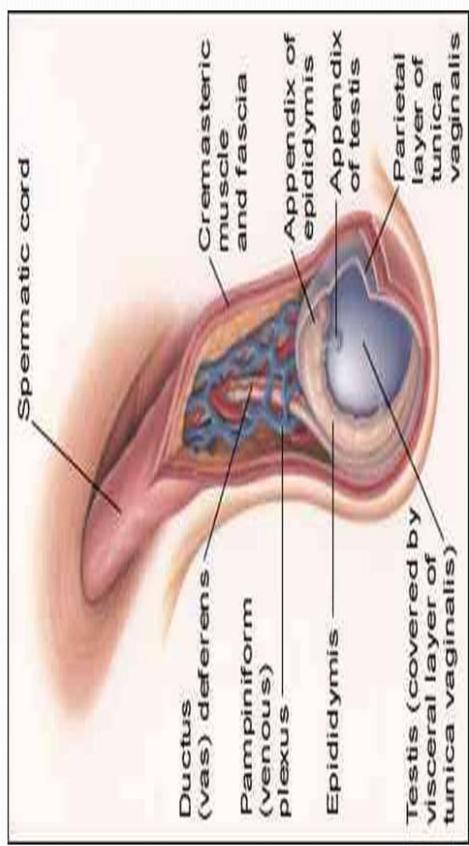
Ureters

- 25cms long
- Retroperitoneal- upper and lower 1/3
- Ureters → pass over pelvic brim at bifurcation of common iliac arteries, in front of the SI joint, run along lateral pelvis wall and enter urinary bladder.
- Three constriction points
 - Jxn of ureter and renal pelvis
 - When ureter crosses brim of pelvic inlet
 - During passage through bladder wall

The following important points of testicular anatomy are true

- a. the testicular arteries are end arteries (F)
- b. the cremasteric reflex is exaggerated in testicular torsion (F)
- c. the hydatid of Morgagni (testicular appendage) is present in 90% of men at the lower pole of the testes (F)
- d. the epididymus is palpated at the posterior of the testes (T)

Testis



Cremasteric Reflex

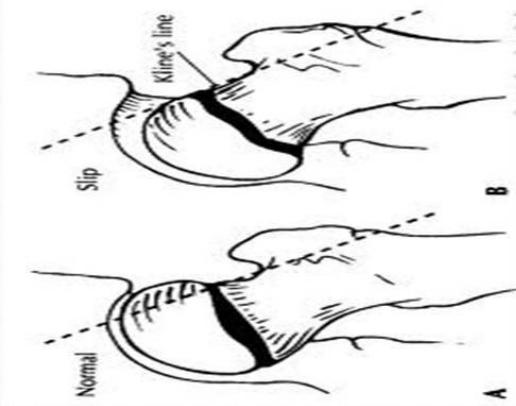
- Superficial reflex observed in human males.
- This reflex is elicited by lightly stroking the superior and medial (inner) part of the thigh.
- The normal response is a contraction of the cremaster muscle that pulls up the scrotum and testis on the side stroked.
- Reflex utilizes sensory and motor fibers of the genitofemoral nerve, formed by fibers from both the L1 and L2 spinal nerves.
- In boys, this reflex may be exaggerated, and this can lead to the mistaken diagnosis of undescended testes.
- Cremasteric reflex may be absent with: testicular torsion, upper and lower motor neuron disorders, as well as a spine injury of L1-L2.
- It can also be lost if the ilioinguinal nerve is accidentally cut during a hernia repair.

Regarding the anatomy of the thoracolumbar spine

- a. the 12th rib articulates with the 12th thoracic vertebra
(T)
- b. the thoraco-lumbar junction is its strongest point
(F)
- c. over 90% of lumbar disc protrusions occur at either L4/L5 or L5/S1 levels.
(T)
- d. rotational movement of the back is largely produced by the lumbar spine
(F)

Slipped upper femoral epiphysis (SUFE / SCFE)

- a. often presents with knee pain
(T)
- b. most commonly occurs in boys aged 5-9 years
(F)
- c. causes the lower leg to internally rotated
(T)
- d. plain X-rays of the hip show the femoral neck displaced anteriorly and superiorly in relation to the femoral head
(F)



SUFE / SCFE

- Often atraumatic or associated with a minor injury
- Most common adolescent hip disorders
- Incidence is 30-60/100,000 children per year.
- Peak age is 13 years for boys and 11.5 years for girls.
- It is three times as common in boys
- Left hip is more commonly affected than the right; it is bilateral in 20-40% of cases.
- Four separate clinical groups are seen:
 - 1) Pre-slip: wide epiphyseal line without slippage.
 - 2) Acute form: slippage occurs suddenly, normally spontaneously.
 - 3) Acute-on-chronic: slippage occurs acutely where there is already existing chronic slip.
 - 4) Chronic: steadily progressive slippage (the most common form).

SUFE / SCFE

- Risk factors
 - Mechanical: local trauma, obesity
 - Hypothyroidism
 - Hypopituitarism
 - GH deficiency,
 - Pseudohypoparathyroidism.
 - AP and frog-leg lateral X-rays show widening of epiphyseal line or displacement of the femoral head
- Complications
 - 1) Chondrolysis
 - 2) Avascular Necrosis
 - Prognosis- depends on the degree of slippage.
 - Less of 1/3- 95% good to excellent results

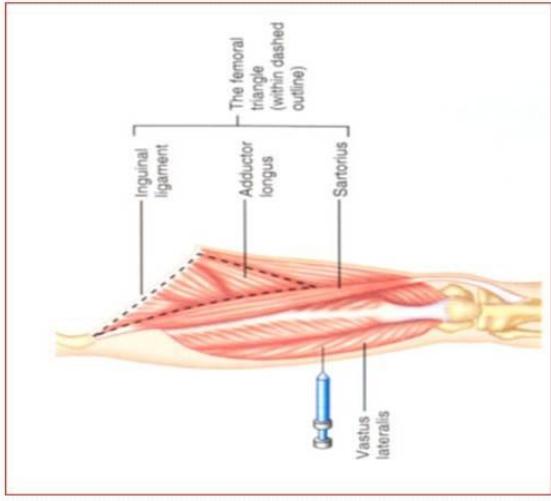
The following are true about the contents of the femoral triangle

- a. the femoral artery can normally be palpated at the base of the femoral triangle 2-3 cm below the midpoint of the inguinal ligament
(T)
- b. the femoral vein lies laterally to the artery
(F)
- c. the femoral nerve supplies motor fibres to the adductors of the hip
(F)
- d. it contains the lateral cutaneous nerve of the thigh
(T)

Regarding the muscles moving the pelvis and hip

- a. rising from a sitting position requires contraction of gluteus maximus
(T)
- b. psoas major flexes and externally rotates the hip joint
(T)
- c. during normal walking gluteus medius and minimus raise the pelvis on the side of the weight-bearing leg
(F)
- d. following mid-shaft fracture of the femur, the proximal fragment is displaced antero-laterally
(T)

Femoral Triangle

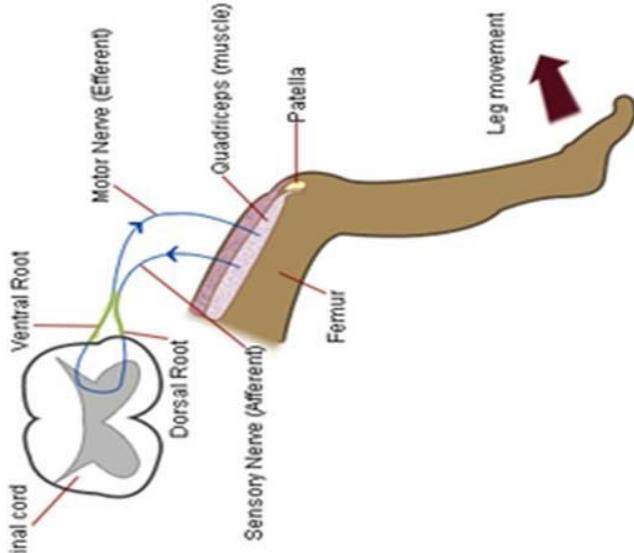


- Femoral Triangle
 - Sartorius (lateral)
 - Adductor longus (medial)
 - Inguinal ligament (superior)
 - Femoral a + v, lymph nodes
 - Gen Fem & Lat Cut. N of Thigh
 - **Mnemonic**, "SAIL" for Sartorius, Adductor longus and Inguinal Ligament

When testing of the deep tendon reflex at the knee (knee-jerk)

- a. the L₂ nerve root is involved
(F)
- b. the reflex arc is polysynaptic
(F)
- c. It may be absent in a tibial nerve palsy
(F)
- d. delayed relaxation may occur with hypothyroidism
(T)

patellar reflex or knee-jerk



Is a deep tendon reflex

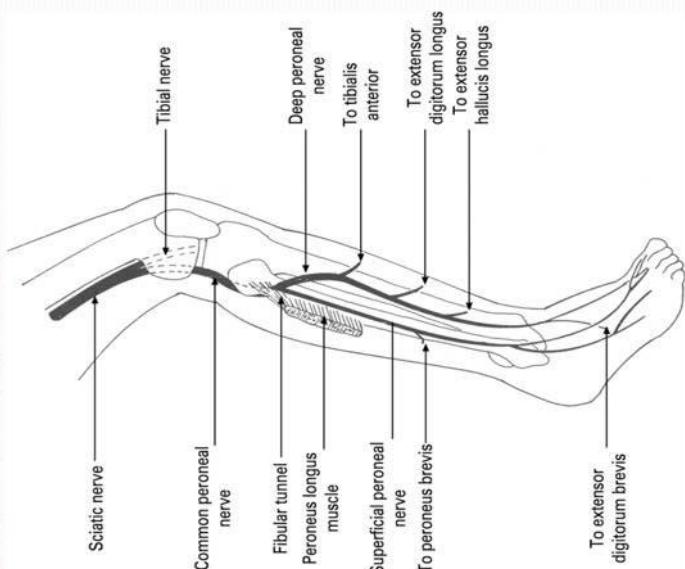
- Is a deep tendon reflex
- It tests L₃-L₄
- There is no **interneuron** in the pathway leading to contraction of the quadriceps muscle.
- Absent stretch reflex indicates a problem within the arc itself- commonly due to peripheral neuropathy
- Slow relaxing reflexes- Hypothyroidism and Hypothermia

With regard to the anatomy of the common peroneal nerve

- a. It receives fibres from both lumbar and sacral nerve roots
(T)
- b. it is closely opposed to the medial condyle of the tibia
(F)
- c. supplies sensation to the skin of the lateral aspect of the lower leg
(T)
- d. injury causes weakness of foot plantar-flexion
(F)

- **Anatomy:** Derived from (**L₄, L₅, S₁, S₂**) as a part of the **sciatic nerve**;
- Supplies short head of **biceps femoris** in thigh,
- Closely opposed to the periosteum of the proximal fibula;
- Divides into superficial & deep peroneal nerves;
- Gives off a lateral sural cutaneous branch which joins with the medial sural cutaneous nerve (from tibial nerve) to form the sural nerve

Common Peroneal Nerve



Peroneal Nerve Palsy

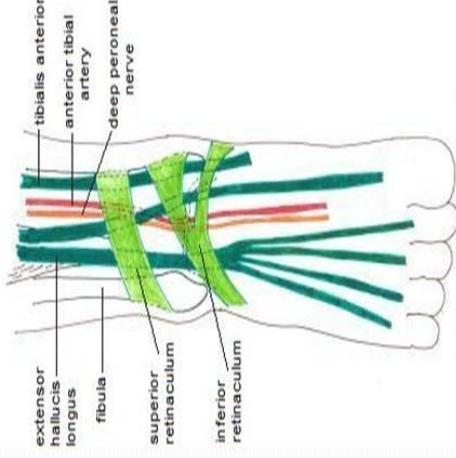
- Clinical syndrome
 - Weakness
 - Foot: Dorsiflexion & Eversion of foot
 - Toes: Extension
 - Gait: Steppage
- Sensory loss
 - Lower leg: Anterolateral
 - Foot & Toes: Dorsum
 - Tendon reflexes: Normal
 - Pain & Tinel's sign: Over lateral fibular neck
- Superficial peroneal
 - Motor
 - Peroneus brevis
 - Peroneus longus
 - Cutaneous sensory
 - Lower leg: Anterolateral
 - Foot: Dorsum, except between 1st & 2nd toes
- Deep peroneal
 - Motor branches in leg
 - Tibialis anterior
 - Extensor hallucis & Extensor digitorum longus
 - Peroneus tertius
 - Lateral terminal branch in foot
 - Extensor digitorum brevis
 - Cutaneous: Skin between 1st & 2nd toes

Structures lying directly beneath the superior extensor retinaculum (transverse crural ligament) of the ankle include

- a. tendon of flexor hallucis longus (F)
- b. tendon of tibialis anterior (T)
- c. deep peroneal nerve (T)
- d. the peroneal (fibular) artery (F)

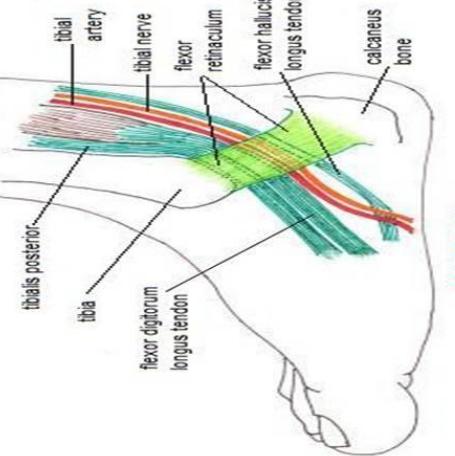
Anterior Tarsal Tunnel Syndrome

- Deep peroneal nerve is compressed below the inferior extensor retinaculum.
- Symptoms - abnormal sensations in the toes and web spaces
- Symptoms increase with walking and running
- More common in runners and athletes.
- It is caused by the formation of a osteophyte (bone spur) in the joints of the foot.
- Diagnosis is by nerve conduction studies



Tarsal Tunnel Syndrome

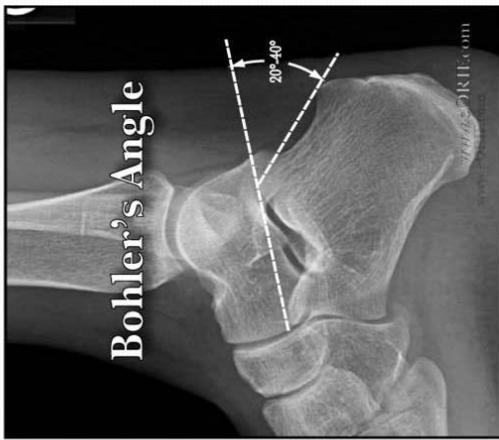
- Causes of compression
 - tenosynovitis
 - tumors
 - rheumatoid arthritis
 - osteoarthritis
 - fractures of the talus, tibia or calcaneum bones
- Abnormal sensation such as tingling and numbness in the sole or toes
- Symptoms may vary throughout the day or with exercise and rest or with position of the limb



In the foot

- a. the tendon of peroneus longus inserts into the base of the 1st metatarsal bone (T)
- b. the long saphenous vein passes posterior to the medial malleolus (F)
- c. Bohler's angle as judged on a lateral foot X-ray should be less than 40 degrees (T)
- d. extension of the big toe is mediated by the L5 and S1 nerve roots (T)

- Measured on lateral x-ray
- Usually between 20° - 40° .
- Formed by lines drawn from the highest point of the anterior process of the calcaneous to the highest point of the posterior facet and a line drawn tangential to the superior edge of the tuberosity.
- Decrease indicates posterior facet has collapsed.



Questions?

- Measured on lateral x-ray
- Seen directly inferior to the lateral process of the talus, formed by lines along lateral border of posterior facet and anteriorly to the beak of the calcaneous.
- Usually between 95° and 105° .



THANK YOU

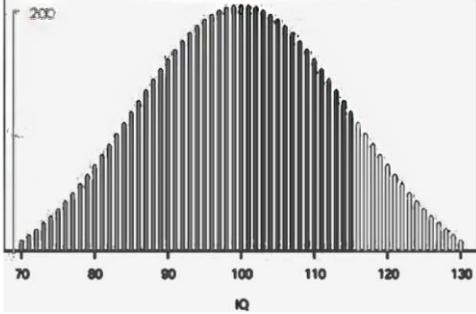
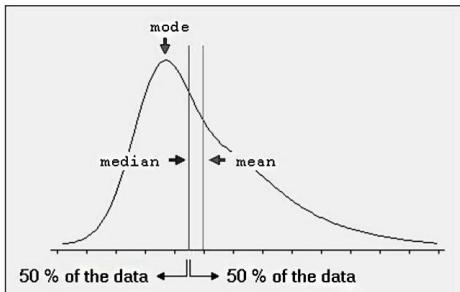
Part 3

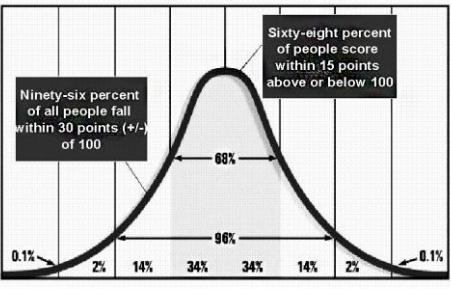
Additional material not given
as lectures

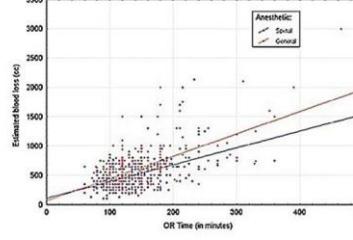
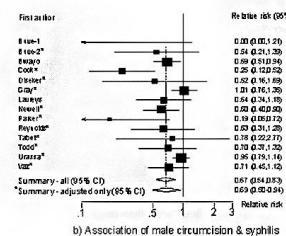
Statistics and Evidence Based Medicine

Hand-out April 2014

This handout should be used in conjunction with the statistics and evidence-based medicine videos on the Bromley Emergency Courses website (www.mcemcourses.org). Under 'Part A resources'.

	Types of data	Unsorted numerical data																																
1	<p>Data</p> <ul style="list-style-type: none"> • Quantitative <ul style="list-style-type: none"> – IQ – Height – BP • Categorical <ul style="list-style-type: none"> – Blood group – Social class 	<p>Data - IQs</p> <table border="1"> <tbody> <tr><td>J Brown</td><td>94</td></tr> <tr><td>T Smith</td><td>115</td></tr> <tr><td>H Philips</td><td>103</td></tr> <tr><td>R Jones</td><td>88</td></tr> <tr><td>D Williams</td><td>121</td></tr> <tr><td>W Green</td><td>86</td></tr> <tr><td>D White</td><td>102</td></tr> </tbody> </table>	J Brown	94	T Smith	115	H Philips	103	R Jones	88	D Williams	121	W Green	86	D White	102																		
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	Organised data – a distribution	The centre of a distribution																																
	<p>Distributions</p> 	<p>Describing distributions - Measures of central tendency</p> <ul style="list-style-type: none"> • Numbers of fillings in 13 children: • 1, 1, 2, 2, 2, 4, 4, 7, 7, 9, 10, 14 • What is the 'average' (or 'typical') • Mode=2 • Median=4 • Mean=5 																																
	Comparing mean, median and mode	Describing spread																																
	<p>Measures of central tendency</p> 	<p>Measures of spread – standard deviation</p> <p>Mean IQ = 101 $SD = \sqrt{(\sum[(x-\text{mean})^2]/n - 1)}$</p> <table border="1"> <thead> <tr> <th>Name</th> <th>IQ</th> <th>Mean - IQ</th> <th>Squared</th> </tr> </thead> <tbody> <tr><td>J Brown</td><td>94</td><td>7</td><td>49</td></tr> <tr><td>T Smith</td><td>115</td><td>-14</td><td>196</td></tr> <tr><td>H Philips</td><td>103</td><td>-2</td><td>4</td></tr> <tr><td>R Jones</td><td>88</td><td>13</td><td>169</td></tr> <tr><td>D Williams</td><td>121</td><td>-20</td><td>400</td></tr> <tr><td>W Green</td><td>86</td><td>15</td><td>225</td></tr> <tr><td>D White</td><td>102</td><td>-1</td><td>1</td></tr> </tbody> </table> <p>Total 1044, divide by 'n-1' (6) = 174, square-root = 13 Therefore standard deviation = 13</p>	Name	IQ	Mean - IQ	Squared	J Brown	94	7	49	T Smith	115	-14	196	H Philips	103	-2	4	R Jones	88	13	169	D Williams	121	-20	400	W Green	86	15	225	D White	102	-1	1
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<h3>Special distributions – the normal distribution</h3>	<h3>Making inferences from a sample</h3>																																								
<h3>Normal distributions</h3>  <p>IQs – normal distribution</p>	<h3>Sampling</h3> <ul style="list-style-type: none"> For practical purposes, we nearly always have to sample (rather than recording from an entire population) Samples must be 'fair' How does our sample relate to the 'true' values of mean and SD for the population? The bigger our sample, the closer the sample mean will be to the population mean 																																								
<h3>How samples are distributed</h3>	<h3>Standard error from a sample</h3>																																								
<h3>Sampling</h3> <ul style="list-style-type: none"> Successive sample means will cluster around the true means, in a predictable way Relationship between sample mean and true mean defined by 'standard error'. Calculated as standard deviation divided by square root of 'n' $SE = SD/\sqrt{n}$	<h3>Comparisons – doctors' IQs</h3> <table border="1"> <thead> <tr> <th>Doctors</th> <th>IQ</th> <th>Mean - IQ</th> <th>Squared</th> </tr> </thead> <tbody> <tr> <td>A</td> <td>118</td> <td>8</td> <td>64</td> </tr> <tr> <td>B</td> <td>135</td> <td>-9</td> <td>81</td> </tr> <tr> <td>C</td> <td>123</td> <td>3</td> <td>9</td> </tr> <tr> <td>D</td> <td>119</td> <td>7</td> <td>49</td> </tr> <tr> <td>E</td> <td>141</td> <td>-15</td> <td>225</td> </tr> <tr> <td>F</td> <td>129</td> <td>-3</td> <td>9</td> </tr> <tr> <td>G</td> <td>120</td> <td>6</td> <td>36</td> </tr> <tr> <td>H</td> <td>122</td> <td>4</td> <td>16</td> </tr> <tr> <td>I</td> <td>126</td> <td>0</td> <td>0</td> </tr> </tbody> </table> <p>Mean IQ = 126, $SD = \sqrt{489/(9-1)} = \sqrt{61} = 7.8$</p> <p>Standard error = $SD/\sqrt{n} = 7.8/\sqrt{9} = 7.8/3 = 2.6$</p>	Doctors	IQ	Mean - IQ	Squared	A	118	8	64	B	135	-9	81	C	123	3	9	D	119	7	49	E	141	-15	225	F	129	-3	9	G	120	6	36	H	122	4	16	I	126	0	0
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<h3>Another sample – are they different?</h3>	<h3>Calculating confidence intervals</h3>																																								
<h3>Lawyers' IQs</h3> <table border="1"> <thead> <tr> <th>Lawyers</th> <th>IQ</th> <th>Mean - IQ</th> <th>Squared</th> </tr> </thead> <tbody> <tr> <td>A</td> <td>115</td> <td>0</td> <td>0</td> </tr> <tr> <td>B</td> <td>124</td> <td>-9</td> <td>81</td> </tr> <tr> <td>C</td> <td>112</td> <td>3</td> <td>9</td> </tr> <tr> <td>D</td> <td>130</td> <td>-15</td> <td>225</td> </tr> <tr> <td>E</td> <td>108</td> <td>7</td> <td>49</td> </tr> <tr> <td>F</td> <td>118</td> <td>-3</td> <td>9</td> </tr> <tr> <td>G</td> <td>110</td> <td>7</td> <td>49</td> </tr> <tr> <td>H</td> <td>111</td> <td>4</td> <td>16</td> </tr> <tr> <td>I</td> <td>107</td> <td>8</td> <td>64</td> </tr> </tbody> </table> <p>Mean IQ = 115, $SD = \sqrt{502/(9-1)} = \sqrt{62.75} = 7.9$</p> <p>Standard error = $SD/\sqrt{n} = 7.9/\sqrt{9} = 7.9/3 = 2.6$</p>	Lawyers	IQ	Mean - IQ	Squared	A	115	0	0	B	124	-9	81	C	112	3	9	D	130	-15	225	E	108	7	49	F	118	-3	9	G	110	7	49	H	111	4	16	I	107	8	64	<h3>Comparisons – confidence intervals</h3> <ul style="list-style-type: none"> 95 % chance that 'true' mean lies within 1.96 standard errors of sample mean Put another way 'true' mean IQ, with 95% confidence lies in the interval $126 \pm (1.96 \times 2.6)$ <p>So</p> <ul style="list-style-type: none"> With 95% confidence 'true' doctors' mean IQ lies between 121 and 131
Lawyers	IQ	Mean - IQ	Squared																																						
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	Calculating confidence intervals	From standard error to 't' test																																									
	Comparisons – confidence intervals <ul style="list-style-type: none"> If we complete the same calculation for lawyers: 95% confidence that 'true' mean IQ for lawyers lies between 110 and 120 	Comparisons – Student's 't' test <ul style="list-style-type: none"> So can we say that doctors have higher IQs than lawyers from these samples? Unlikely that both 'true' mean of lawyers' IQ and of doctors' IQs are at extremes. In practice if means are more than about two standard errors apart, there is a 95% confidence that there is a 'true' difference. In small samples the number of SEs has to be increased slightly to allow for increased chance of sampling error, the exact figure is known as 't'. 																																									
	Comparing means	Comparing continuous variables																																									
	Statistical tests <ul style="list-style-type: none"> For groups of continuous data Normally distributed <ul style="list-style-type: none"> Student's 't' test (two groups) ANOVA Non-parametric <ul style="list-style-type: none"> Mann-Whitney U test Wilcoxon rank sum test 	Comparison of two continuous variables  <p>Normally distributed: Pearson's correlation coefficient Non-parametric: Spearman's rank correlation</p>																																									
	Comparing proportions	Combining many studies																																									
	Comparing proportions <p>GROUP * CHOICE Crosstabulation</p> <table border="1"> <thead> <tr> <th colspan="2" rowspan="2"></th> <th colspan="2">CHOICE</th> <th rowspan="2">Total</th> </tr> <tr> <th>art degree</th> <th>science degree</th> </tr> </thead> <tbody> <tr> <th rowspan="2">GROUP</th> <th>boys</th> <td>Count</td> <td>25</td> <td>50</td> <td>75</td> </tr> <tr> <th></th> <td>Expected Count</td> <td>40.0</td> <td>35.0</td> <td>75.0</td> </tr> <tr> <th rowspan="2"></th> <th>girls</th> <td>Count</td> <td>55</td> <td>20</td> <td>75</td> </tr> <tr> <th></th> <td>Expected Count</td> <td>40.0</td> <td>35.0</td> <td>75.0</td> </tr> <tr> <th>Total</th> <td>Count</td> <td>80</td> <td>70</td> <td>150</td> <td></td> </tr> <tr> <th></th> <td>Expected Count</td> <td>80.0</td> <td>70.0</td> <td>150.0</td> <td></td> </tr> </tbody> </table> <p>Chi squared test: $\sum(O-E)^2/E$ (where O=observed, E=expected)</p>			CHOICE		Total	art degree	science degree	GROUP	boys	Count	25	50	75		Expected Count	40.0	35.0	75.0		girls	Count	55	20	75		Expected Count	40.0	35.0	75.0	Total	Count	80	70	150			Expected Count	80.0	70.0	150.0		Meta-analysis <ul style="list-style-type: none"> Combines results from several studies Forrest plot Heterogeneity  <p>Relative risk (95% CI)</p> <p>Studies included: Euse-1 Euse-2* Euse-3 Euse-4 Euse-5 Garg* Lalvani* Meehan* Parker* Perry* Teele* Todd* Uzarraga* Van Summary: all (95% CI) Summary: adjusted only (95% CI) </p> <p>b) Association of male circumcision & syphilis</p>
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Type 1 and type 2 errors	Type 1 and type 2 errors
<p>Type I and Type II error</p> <p>When we use a statistical test, there is a chance that the decision we make with it is a wrong one</p> <p>We either accept or reject our hypothesis on a chance score (($p<0.05$ or $p<0.01$) a 1 in 20 chance or a 1 in 100 chance)</p> <p>Occasionally these chances will be wrong, either a Type I error or a Type II error</p>	<p>Type I and Type II error</p> <p>Type I error – The possibility of rejecting the null hypothesis given that it is true, or believing in an effect where there is not one</p> <p>Type II error – failing to reject the null hypothesis when it is not true, there is an effect but we have not found it in this experiment – so we say there is not one</p>
Clinical and statistical significance	Power of a study
<ul style="list-style-type: none"> clinical significance: A conclusion about whether or not an observation is of practical meaning to patients and health care providers. To illustrate a type of treatment might be found to have a statistically significant effect on a group of patients, but the effect might not have any practical importance. statistical significance Statistical significance indicates the probability that the observed difference was due to chance (if the null hypothesis is true). If the probability is less than 5% (by convention), then the null hypothesis is rejected 	<p>Power and sample size</p> <ul style="list-style-type: none"> The probabilities of type I and type II errors are α and β α relates to the p value, generally 5% β depends on the size of the effect of interest and the sample size. $\text{Power} = 1 - \beta$ Power can be set in advance through an appropriate sample size
Calculating power using a nomogram	Controlled trial terminology
<p>Standardised difference (left axis) is the ratio of the difference of interest to the standard deviation</p>	<p>RCT terms</p> <ul style="list-style-type: none"> double blind: A clinical trial in which the method for analysing data had been specified in the protocol before the study has begun, the patients have been randomly assigned to receive either the study drug or alternative treatment, and in which neither the patient nor the clinicians(s) conducting the study know which treatment is being given to the patient.

Controlled trial terminology	Quantitative research										
<ul style="list-style-type: none"> • cross-over study: A study in which every patient receives each of the treatments involved in the study, preferably in a different random order. Treatment comparisons are made within each patient. • washout period: The period between two active treatments during which the patient receives only placebo medication. The purpose of a washout period is to remove all traces of the first drug from the patient before the second active treatment is started. 	<ul style="list-style-type: none"> • qualitative research: Collection of non-numerical data using interviews, observations, and open-ended questions to gather meaning from non-quantified narrative information. • quantitative research: Collection of numerical data in order to describe, explain, predict, and/or control phenomena of interest. 										
Evidence based medicine terms	Evidence based medicine terms										
<p style="text-align: center;">EBM</p> <p>Some evidence based medicine terms</p> <p>EER = Experimental event rate CER = Control event rate</p> <p>Absolute and Relative Risk Reduction ARR = EER-CER RRR = (EER-CER)/CER</p>	<ul style="list-style-type: none"> • Relative Risk Reduction = EER-CER /CER • Say the disease A occurs in 1 in 100,000 people but taking drug X reduces the incidence to 1 in 10,000,000. The absolute risk of disease is 0.001%. The relative risk is 0.00001/0.001 = 0.1 and the relative risk reduction is 1 - 0.1 = .9 or 90% while the absolute risk reduction is 0.00001 - 0.001 = -0.00099 or 0.099%. • In contrast, disease B has a mortality rate of 50% and drug Y reduces mortality from 50% to 40%. The absolute risk of death with disease B is .5 or 50% and the relative risk is .4/.5 = 0.8 or 80%. The relative risk reduction is 1-0.8 = 0.2 or 20% while the absolute risk reduction is 0.4-0.5 = .1 or 10%. In this case the relative risk reduction is 20% 										
Evidence based medicine terms	NNT examples										
<ul style="list-style-type: none"> • NNT (Number Needed to Treat): The number of patients who need to be treated to prevent 1 adverse outcome. (The treatment, its duration, and the adverse outcome being prevented must be specified). Reported as a whole number, calculated as 1/ARR, rounded to the next highest whole number, and accompanied by its 95% confidence interval (CI). e.g. 1/ARR = 1/6.8% = 14.7, rounded to 15, with a 95% CI from 9 to 35. 	<p style="text-align: center;">Number Needed to Treat (NNT) to prevent one recurrent stroke</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: center;">Agent</th> <th style="text-align: center;">NNT</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">1. Clopidogrel</td> <td style="text-align: center;">125</td> </tr> <tr> <td style="text-align: center;">2. Ticlopidine</td> <td style="text-align: center;">40</td> </tr> <tr> <td style="text-align: center;">3. Aspirin/extended release dipyridamole</td> <td style="text-align: center;">33</td> </tr> <tr> <td style="text-align: center;">4. Perindopril</td> <td style="text-align: center;">23</td> </tr> </tbody> </table>	Agent	NNT	1. Clopidogrel	125	2. Ticlopidine	40	3. Aspirin/extended release dipyridamole	33	4. Perindopril	23
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	<ul style="list-style-type: none"> Likelihood Ratio: The likelihood that a given test result would be expected in a patient with a disease compared to the likelihood that the same result would be expected in a patient without that disease. Likelihood Ratio Positive (LR+): The odds that a positive test result would be found in a patient with, versus without, a disease. Likelihood Ratio Positive (LR+) = Sensitivity / (1 - Specificity). The probability of a test result being positive in a person with the disease divided by the probability of a test result being positive in a person without the disease. $LR(+) = [TP / (TP + FN)] / [FP / (FP + TN)]$ 	<h3>Likelihood ratios</h3> <ul style="list-style-type: none"> $LR+ > 10$: Useful test (as long as pre-test probability 33% or more) $LR- < 0.1$: Useful test to exclude a diagnosis (if pre-test probabilities < 33%) 																																										
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RENAL PHYSIOLOGY: FLUID & ELECTROLYTE BALANCE

Handout – April 2014

The first two pages cover the current curriculum for renal physiology published by The College of Emergency Medicine in June 2010

Curriculum for renal physiology is as follows:

Functional anatomy of the renal tract

Note: you should cross-reference this section with the anatomy curriculum

Macroscopic structure of the kidney:

- Cortex + medulla and the principal components of each [e.g. location of glomeruli]
- Composition of the nephron [Bowman's capsule, tubules etc]
- Function [in broad terms] of each component of the nephron
- Appreciation of how nephron anatomy reflects these functions

Renal blood supply and drainage:

- Appreciation of the rich vascularity of the kidney and the rationale for this
- Structural arrangement of afferent and efferent arterioles
- Importance of renal autoregulation and a simple overview of factors affecting it

Mechanism of filtration in health

Glomerular filtration:

- Normal GFR and filtration fraction in adults
- The three glomerular filtration barriers and the importance of molecular size
- Factors affecting GFR [Starling forces, relative arteriolar resistance]
- The role of vasoactive substances in affecting GFR

Creatinine clearance:

- Understanding of why creatinine is chosen for the clearance calculation
- Knowledge of the equation $(\text{Cu} \times \text{V}) / \text{Cp}$ in calculating clearance
- *Knowledge of inulin and PAH as function indices is not required*

Tubular transport:

- Available modes of tubular transport [paracellular and transcellular]
- Simple understanding of the difference between primary + secondary active transport
- Concept of maximal tubular transport and implications for glucose threshold
- Plasma level of glucose above which splay and saturation occur

Proximal tubular function:

- Appreciation of the principal agents reabsorbed at this site
- Understanding of the particular dynamics of sodium and glucose in this region

Loop of Henle:

- Primary functions of the thin and thick limbs
- Importance of the counter-current multiplier
- Effect of loop diuretics upon thick limb symporters

Distal collecting system:

- Water permeability of this region and the effect of ADH upon water + urea handling
- Role of urea in maintenance of medullary osmolality
- Relation of potassium excretion to tubular flow and the implication for diuretic therapy
- Roles of PTH and activated Vitamin D in the handling of calcium in this region

Regulation of plasma osmolality:

- Overview of regulatory mechanism [hypothalamus, ADH, thirst, feedback loop]
- Effects of ADH upon vascular tone systemically and renally
- Sites of metabolism of ADH and appreciation of its rapid removal via feedback

Effects of renal hormones:

- Angiotensin II as the principal agent in sodium balance
- Role of ACE in generating angiotensin II
- Effects of angiotensin II on vessels, tubules, hypothalamus, adrenal cortex
- Positive and negative feedback effects of angiotensin II
- Effects of aldosterone and ANP in health

Acid – base balance

Normal values:

- Normal range of arterial blood pH and the importance of maintenance of this range
- Henderson-Hasselbach equation for bicarbonate and CO₂ equilibrium
- The anion gap – components and calculation

Metabolic disturbance:

- The typical ABG features of metabolic + respiratory alkalosis and acidosis
- An understanding of the primary systemic compensations which occur in each type

Renal regulation of acid – base balance:

- Urinary acidification [bicarbonate reabsorption + acid formation + handling of ammonia]
- The kidneys as net renal excretors of acid
- Factors influencing renal secretion and excretion of hydrogen ions

Potassium balance

Normal values:

- Intracellular and extracellular normal potassium concentrations

Effect of disordered potassium balance:

- The main clinical effects of hypo- and hyper- kalaemia, including ECG effects
- The handling of potassium through the renal tract:
- Influence of aldosterone, acid – base disturbance, sodium excretion

Calcium balance [see also Section 6 below]

Normal values:

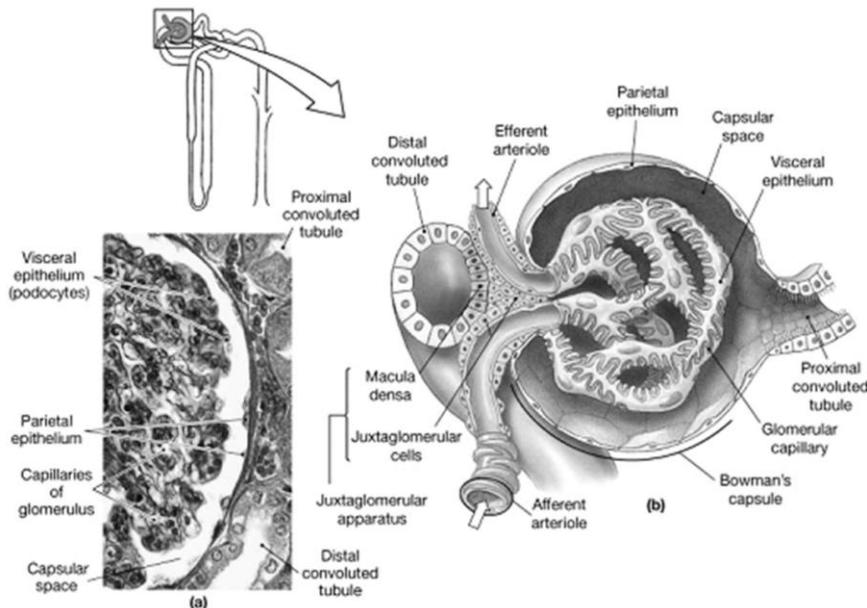
- Normal values of calcium and the rationale for corrected calcium values

Sources and handling of calcium:

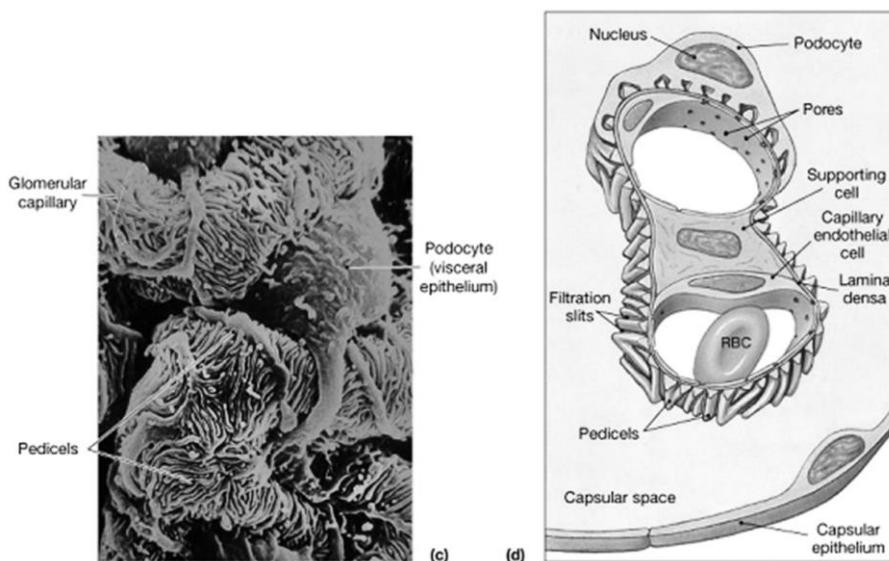
- Foodstuffs rich in calcium
- Sites of calcium transfer along the nephron in health
- Effect of PTH upon renal calcium handling

Functional Anatomy

The components of the nephron



The podocytes and capillary structure and filtration



Filtration

20% of cardiac output passes through the kidneys.

In the glomerulus filtration produces bulk transport of fluid through the 'filter'

High pressure in glomerular capillaries (60% of MAP)

20% of glomerular plasma flow passes through the 'filter' (filtration fraction). Reminder of renal blood flow moves on to flow around tubules etc.

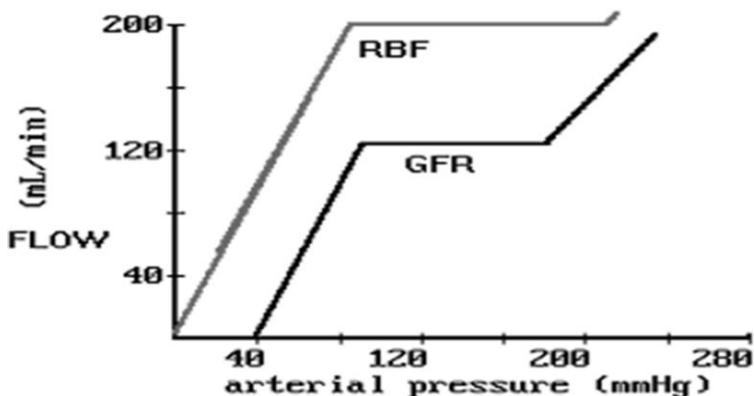
Basement membrane is 'porous'

- (allows anything through smaller than 10,000, some molecules up to 100,000 atomic mass)

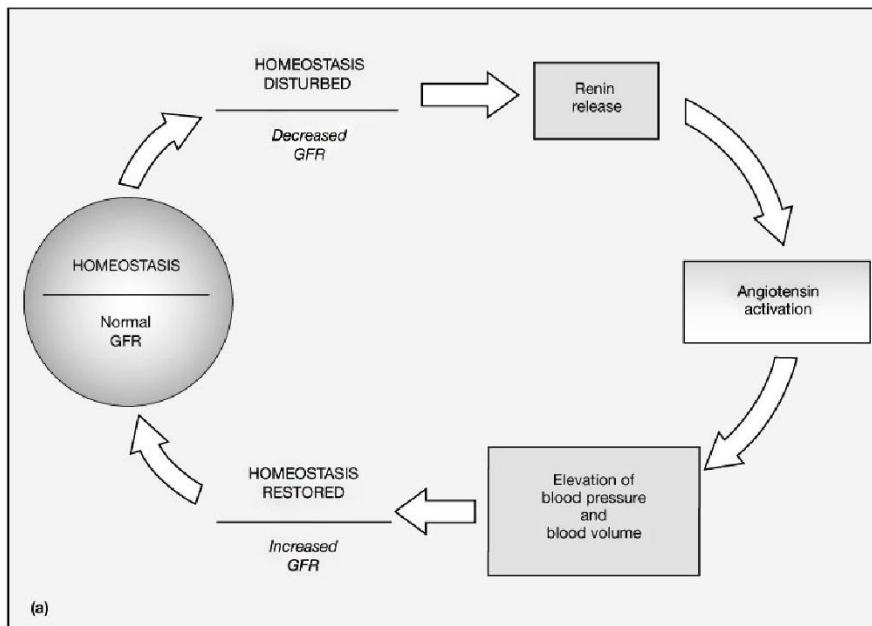
The filtrate is isosmotic, and total flow through the filter equals 180 litres/day (the glomerular filtration rate, GFR)

Autoregulation of GFR

The GFR is largely independent of systemic blood pressure



Renin is partially responsible for homeostasis of GFR



Clearance and GFR

GFR is a clinically important measure but cannot be measured directly easily.

In practice different chemicals are excreted by the kidneys at different rates because excretion is not only dependent on GFR, but also on tubular cell handling of the chemical in question. Hence 'clearance' for a chemical.

Amount cleared from filtered plasma in unit time = amount appearing in urine

Therefore, for a substance that is filtered only, in any period of time:

$$\text{GFR} \times \text{plasma concentration} = \text{urine concentration} \times \text{urine volume}$$

OR

$$\text{GFR} = \{U \times V\}/P$$

Creatinine can be used to estimate GFR (as little tubular excretion)

Inulin is even better

For any substance, if no tubular excretion or absorption, clearance = GFR

However absorption or excretion can reduce or increase the clearance

Reabsorption in proximal tubules

Process of returning filtered material to the bloodstream

99% of what is filtered is returned

There are many mechanisms (not all well understood), eg for:

- Solutes, Na, K, Cl, glucose
- Amino acids
- Proteins

Aided by large surface area for absorption (brush border etc)

Normally glucose is totally reabsorbed (but saturable, above serum concentration of about 10mmol/l)

Ketones (ketoacids) usually reabsorbed (but also saturable)

Secretion by the tubules

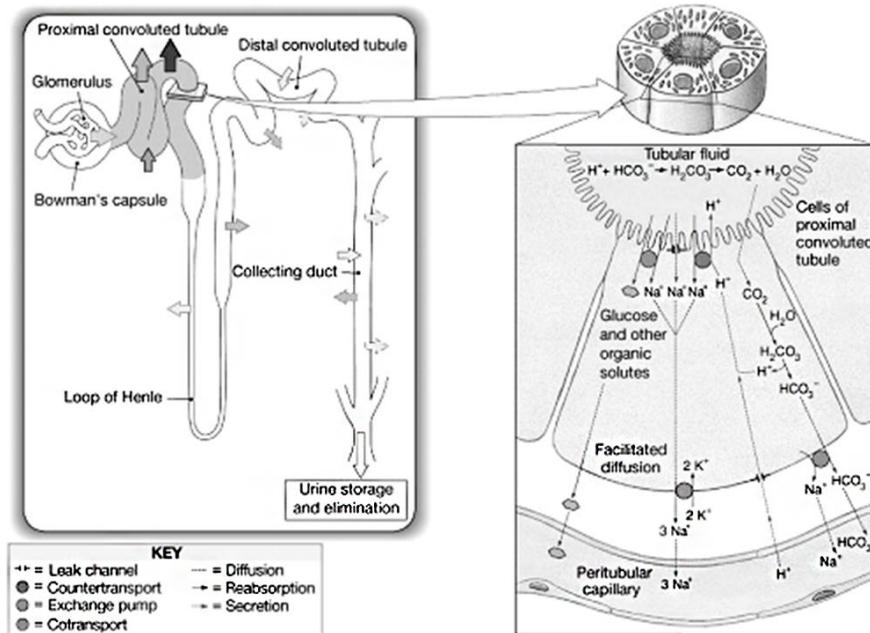
Many chemicals secreted by tubules

- eg salicylate, penicillin, frusemide

Separate pathways for anions and cations

PAH (para-amino hippurate) completely secreted from tubular capillary plasma (when at low concentrations).

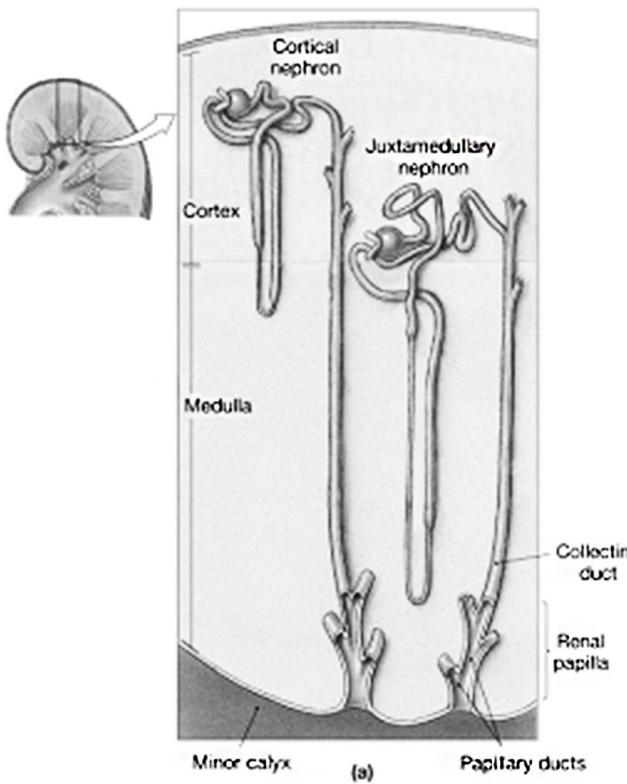
- So PAH clearance = renal plasma flow



Loop of Henle

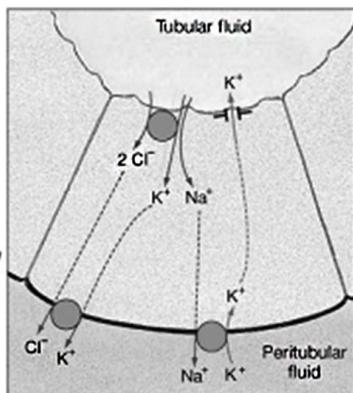
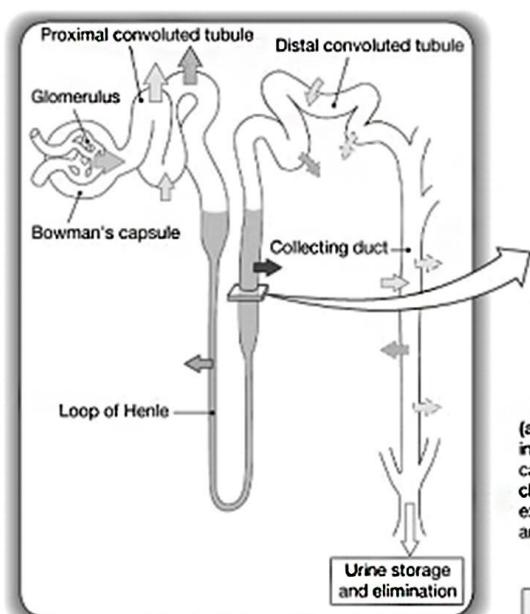
- 20% of nephrons have loops that run deep into medulla

- Osmolarity increases from 285 mosm/l to 1200 mosmol/l on descending into depth of medulla (Na and urea equal contributors to this)
- High osmotic gradient is due to active processes in the loop
- 25% of Na reaching loop remains in medulla, while associated water moves on, back to cortex
- Fluid reaching distal tubule is hypotonic



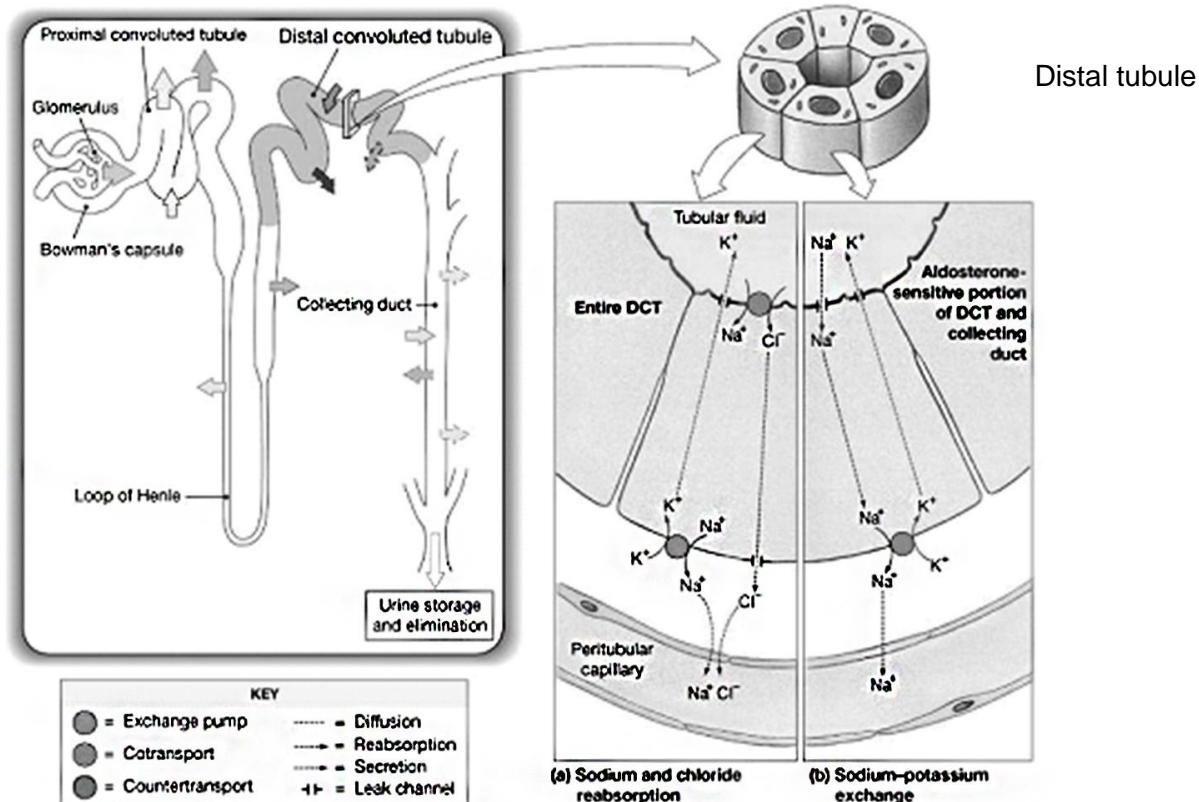
Cortical and juxamedullary nephrons (which run deep into the medulla and create the hypertonic environment in the deep medulla)

Sodium/potassium ATPase



(a) The mechanism of sodium and chloride ion transport involves $\text{Na}^+-\text{K}^*/2\text{Cl}^-$ carrier at the apical surface and two carriers at the basal surface of the tubular cell: a potassium-chloride cotransport pump and a sodium-potassium exchange pump. The net result is the transport of sodium and chloride ions into the peritubular fluid.

KEY	
● = Cotransport	----- = Diffusion
● = Exchange pump	→ → = Reabsorption
→ ← = Leak channel	→ ← = Secretion

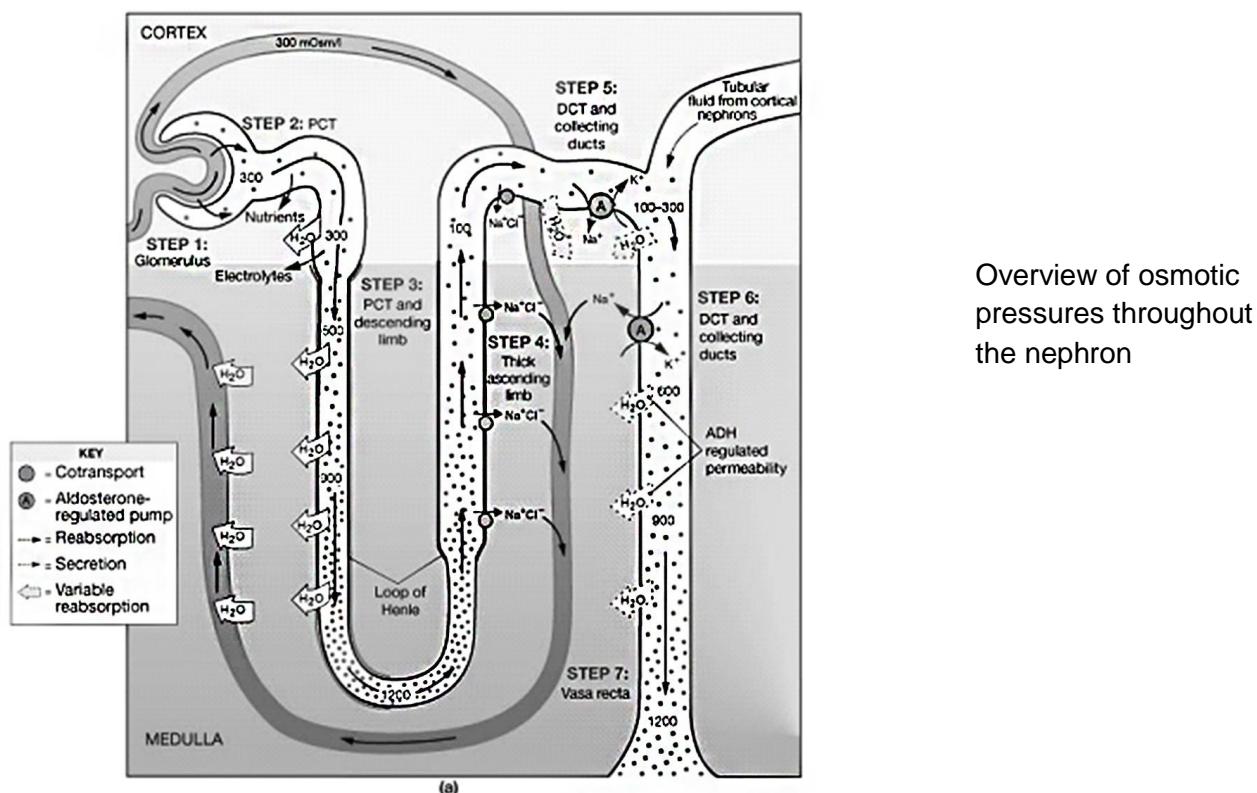


Distal tubule

- Has feedback control of afferent arteriole smooth muscle (to control rate of filtration – see renin above)
- More reabsorption of Na and water occurs
- Na exchanged for potassium (aldosterone controlled)

Collecting duct

- Receives hypotonic fluid from DCT
- Action of ADH opens channels, powerful osmotic gradient reabsorbs water
- No water reabsorption without ADH



Specific functions of the kidney

Control of water/osmolarity

Water loss (normal conditions)

- Urine (1.5 L/day)
- Faecal matter (100 mL/day)
- Evaporative loss through skin & respiration (900 mL/day)

Total body water = 0.6 x body wt.
(36 L)

is divided into:

Extracellular Fluid (ECF) Intracellular Fluid(ICF)

0.2 x body wt. 0.4 x body wt.

= 12L = 24L

ECF is then divided into:

Interstitial fluid (ISF) Plasma

3/4 ECF 1/4 ECF

= 9 L = 3 L

Total Body Water

1. varies depending on body fat:
2. infant: 70%
3. male adult: 60%
4. female adult: 50%
5. effects of obesity, age

Control of water/osmolarity

- *Thirst*
- *ADH*

Anti-diuretic Hormone

Released when body fluid osmolarity increases (greater than 280+):

Mechanism of action:

Osmoreceptors (hypothalamus) trigger:

Thirst and:

Release of ADH

Which increases permeability of CD to water

Causes water reabsorption from tubule

Concentrated urine produced

Osmolarity/osmolality

Definitions: osmolality is number of particles per Kg of solvent, osmolarity is per litre of solution. In human physiology the numbers are very similar.

Quick approximation

Serum: 2 x (Na + K) + urea + glucose

- Normal 275-295

Urine

- Normal range 50 – 1200 mOsmol/Kg

Urine osmolality and renal disease.

(In pre-renal renal failure, kidney endeavours to concentrate, and conserve sodium), these mechanisms fail in intrinsic kidney disease

	Pre-renal uraemia	Acute tubular necrosis or intrinsic renal disease
Urine osmolality	>500	<350
Urine sodium	<20	>40
Urine sediment	Bland	Muddy brown granular casts

Water Movement

In water deficit:

Equilibration of water loss with intracellular fluid throughout the body

- Cells shrink (ultimately coma)

In water excess:

Cells enlarge, raised ICP

- Confusion, headache, vomiting, coma

Regulation of Sodium

Total body sodium is linked to circulating volume

So body sodium sensed through sensing circulating volume

- Stretch receptors in atria - neural paths
- Juxtaglomerular apparatus - renin etc

Renin/ angiotensin system

Angiotensinogen (from liver)

Cleaved by renin in the circulation to:

angiotensin I

Converted in lungs to:

angiotensin II

Acts on adrenal cortex to release:

Aldosterone (plus thirst, ADH)

Sodium regulation

Relatively slow system to respond.

In response to low body sodium:

- Aldosterone promotes sodium reabsorption
- Neural pathways influence GFR and other mechanisms

In response to high sodium – natriuretic peptides

Potassium balance

- Potassium can be both reabsorbed and secreted in distal tubular cells
- Sodium exchanged for potassium in DCT in response to aldosterone

Acid/base balance

- All hydrogen ions produced by metabolism are buffered with bicarbonate, becoming water and CO_2 .
- Bicarbonate is replaced by production in the renal tubular cells by carbonic anhydrase
- Equivalent amount H^+ transported into tubular lumen
- H^+ buffered and passed out in the urine

Calcium Metabolism

- Homeostasis maintained by hormonal controls on gut, bone and kidney
- PTH acts on kidney to increase absorption Ca (ascending loop and DCT) raises serum calcium concentration.
- Vit D increases total body Ca through action on gut, but does not control serum calcium concentration.
- Calcitonin is less important – reduces serum Ca level.



MCEM PART A – Clinical chemistry- 5 MCQs

CLINICAL BIOCHEMISTRY

MCEM Part A

Fm Loker N.

Dr Chet Trivedy
BDS FDS RCS (Eng) MBBS PhD MCEM
LEARN Research Fellow

CURRENT MCEM A SYLLABUS

- Control of energy production
- Metabolic responses to stress including injury, infection, infarction, temperature, burns
- Acid – base control
- Glucose
- Lactate
- Plasma hormone concentration
- Liver function test
- Anion gap and causes of abnormalities
- Arterial blood gases



IV CRYSTALLOIDS...



The following are true of the composition of intravenous fluids

- a. 0.9% saline contains 150mmol of chloride in each litre
- b. Hartmann's solution contains both hydrogen carbonate and potassium
- c. dextrose saline contains 0.25% saline in 4% dextrose
- d. the typical daily requirement of sodium is 80mmol for the average adult

Electrolyte concentrations—intravenous fluids

Intravenous infusion	Na ⁺	K ⁺	HCO ₃ ⁻	Cl ⁻	Ca ²⁺	Millimoles per litre
Normal plasma values	142	4.5	26	103	2.5	
Sodium Chloride 0.9%	150	—	—	150	—	
Compound Sodium Lactate (Hartmann's)	131	5	29	111	2	
Sodium Chloride 0.18% and Glucose 4%	30	—	—	30	—	
Potassium Chloride 0.3% and Glucose 5%	—	40	—	40	—	
Potassium Chloride 0.3% and Sodium Chloride 0.9%	150	40	—	190	—	
<i>To correct metabolic acidosis</i>						
Sodium Bicarbonate 1.26%	150	—	150	—	—	
Sodium Bicarbonate 8.4% for cardiac arrest	1000	—	1000	—	—	
Sodium Lactate (m/6)	167	—	167	—	—	BNF 2010



The following are true of the composition of intravenous fluids

- a. 0.9% saline contains 150mmol of chloride in each litre **T**
- b. Hartmann's solution contains both hydrogen carbonate and potassium **T**
- c. dextrose saline contains 0.25% saline in 4% dextrose **F**
- d. the typical daily requirement of sodium is 80mmol for the average adult **T**



Hyponatraemia

- a. Is a feature of Conn's syndrome
- b. The urine sodium is concentrated where SIADH is the cause
- c. Central pontine myelinosis results at plasma sodium levels below 115mmol/l
- d. Very commonly causes confusion in the elderly **T**



Hyponatraemia

- a. Is a feature of Conn's syndrome **F**
- b. The urine sodium is concentrated where SIADH is the cause **T**
- c. Central pontine myelinosis results at plasma sodium levels **F** below 115mmol/l
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Hyponatraemia...

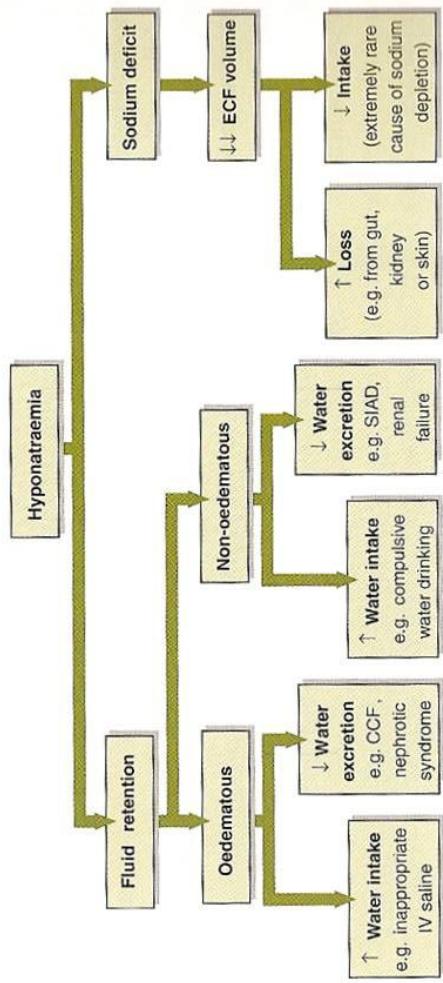


Fig. 1 The causes of hyponatraemia.



**Which of the following are true regarding
Troponins**

- Are present in skeletal muscle
- serum troponin levels are only raised in acute MI
- serial measurement of troponin T is needed for the confirmation of acute MI
- mild elevation of troponin T in angina patients indicates a poorer prognosis
- a normal troponin on admission excludes MI

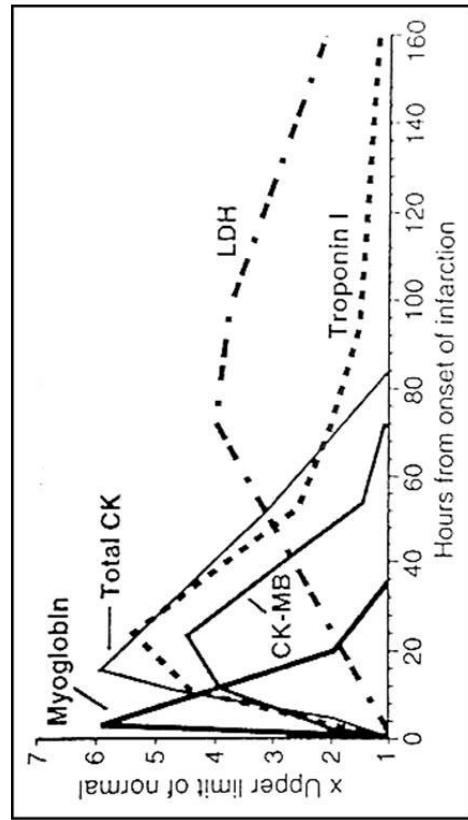
- Troponin C & T is found in skeletal muscle
- Trop-T (biphasic) & Trop-I (single peak)
- Trop-I **ONLY FOUND** in myocardium
- Can be elevated for up to 2 weeks post MI
- cTnI considered to be most specific with several assays
- Diagnostic sensitivity approaches 100% at 12 hours (but does rise earlier in MI)
- ↑ Trop also occurs in
 - Myo/pericarditis
 - PE
 - Renal failure



Know the enzyme timeline...

**Which of the following are true regarding
Troponins**

- Are present in skeletal muscle **T**
- serum troponin levels are only raised in acute MI **F**
- serial measurement of troponin T is needed for the confirmation of MI **F**
- mild elevation of troponin T in angina patients indicates a poorer prognosis **T**
- a normal troponin on admission excludes MI **F**





Regarding hypercalcæmia

- a. Tetany is a feature F
- b. A raised ALP suggests haematological malignancy is the cause
- c. Is a cause of vomiting
- d. rarely gives polyuria and dehydration



HypErcalcaemia...

- Stones , bones, abdominal groans, psychic moans...
- Calcium regulation: parathyroid hormone (PTH), 1,25-dihydroxyvitamin D (calcitriol), and calcitonin (bone, kidney, small intestine)
- Commonest cause in UK is due to metastatic disease in bone and parathyroid adenoma (primary hyperparathyroidism), also sarcoidosis, xs vit D
- Calcium >3.5mmol/l is **life threatening**
- Treat with iv fluids and bisphosphonates
- Disrupts intestinal smooth muscle contraction by binding with intracellular calmodulin



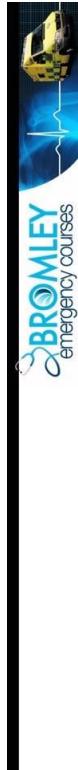
Regarding hypercalcæmia

- a. tetany is a feature F
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- c. Is a cause of vomiting T
- d. rarely gives polyuria and dehydration F



Hypocalcaemia

- Tetany, depression, *perioral paraesthesia, *carpopedal spasm (Trousseau, Chvostek) * occurs in hyperventilation because ionised calcium ↓
- Causes
 - Thyroid/ Parathyroid surgery,
 - if PO4↑ - CRF, hypoparathyroidism, rhabdomyolysis
 - if PO4↓ or normal, osteomalacia, over-hydration, pancreatitis
- 40% calcium is bound to albumin
- Treat with with IV Calcium gluconate





Vomiting & Diarrhoea...

Abnormalities in the vomiting patient commonly include

- a. urea 19
- b. K 2.6
- c. Cl 85
- d. Na 126
- e. pH 7.49



- Sodium can fall if predominantly diarrhoea
- Hypokalaemic hypochloraemic alkalosis- vomiting++ (bulimia)
- Treat the underlying cause

Electrolyte content—gastro-intestinal secretions

Type of fluid	Millimoles per litre			
	H ⁺	Na ⁺	K ⁺	HCO ₃ ⁻
Gastric	40-60	20-80	5-20	—
Biliary	—	120-140	5-15	30-50
Pancreatic	—	120-140	5-15	70-110
Small bowel	—	120-140	5-15	20-40
				90-130



Regarding hypoglycaemia

- a. may be caused by strenuous exercise
- b. causes reduced secretion of insulin
- c. may be caused by alcohol through inhibition of the glycolysis
- d. urinary ketones are often found in well individuals

Abnormalities in the vomiting patient commonly include

- a. urea 19 T
- b. K 2.6 T
- c. Cl 85 T
- d. Na 126 F
- e. pH 7.49 T





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Hypoglycaemia- causes...

Exogenous drugs

Pituitary insufficiency

Liver failure

Addisons disease

Islet cell tumours

Non- pancreatic neoplasms

OHCM 2007



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Hypoglycaemia

- Is a **life threatening** condition
- If prolonged can cause neuroglycopenic brain damage (cerebral oedema)
- Current practice is to treat with 10-20% glucose iv
- 50% glucose should be given through a CVP line only
- Beware T2DMs who are likely to suffer symptoms of hypoglycaemia at higher BMs



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Hypoglycaemia

- a. may be caused by strenuous exercise **T**
- b. causes reduced secretion of insulin **T**
- c. may be caused by alcohol through inhibition of the glycolysis **F**
- d. urinary ketones are often found in well individuals **T**



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↑CK....

- Elderly- prolonged time on the floor
- Trauma- especially crush injuries and burns/burns/electrocution
- Be aware of the treatment and management of rhabdomyolysis (myoglobinuria ‘coca-cola urine’)
- Statins are an often overlooked cause of a raised CK
- Hypothyroidism can → myopathy, CK can be 20 times normal



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The causes of a raised CK include

- a. polymyositis T
- b. strenuous exercise T
- c. hyperthyroidism F
- d. delirium tremens T
- e. 3-4 methylenedioxymethamphetamine T



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CSF...

Consider the following statements regarding cerebrospinal fluid

- Produced in the choroid plexus (400-500mls/day)
- Be aware of the CSF parameters both normal and abnormal (SAH, infection, TB, MS)
- Typically <5 cells/ml
- Opening pressure on LP is 15-20mmHg
- Xanthochromia best detected 12 hours post headache & is present in around 70% at 3 weeks
- Research is ongoing with CSF D-Dimers
- CSF leak can be identified with glucostix or litmus paper (check plasma BM also)



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Consider the following statements regarding cerebrospinal fluid

- a. The volume is around 130mls **T**
- b. opening pressure typically 30cmH₂O when lumbar puncture is performed on the supine patient
- c. Typically less than 100 cells/ml **F**
- d. Xanthochromia is best detected 4 hours post onset of headache in a suspected SAH **F**



Consider the following statements regarding the biochemistry of hyperuricaemia

- a. most cases of gout result from increased production of uric acid
- b. it is a disorder of purine metabolism
- c. loop diuretics can prevent gout
- d. polycythaemia is a cause **F**



Hyperuricaemia...

- prevalence of gout is 0.2%
- hyperuricaemia in this population occurs in about 5%.
- Gout can occur in normouricaemics.
- Lesch-Nyhan syndrome, Kelley-Seegmiller Syndrome-HGPRT
- Diuretics can precipitate gout
- Can occur where there is rapid cell proliferation eg polycythaemia, leukaemia, myeloproliferative disorders.



Consider the following statements regarding the biochemistry of hyperuricaemia

- a. most cases of gout result from increased production of uric acid **F**
- b. it is a disorder of purine metabolism **T**
- c. loop diuretics help prevent gout **F**
- d. polycythaemia is a cause **T**

DKA...

Regarding the biochemistry of diabetic ketoacidosis

- there is impaired glucose uptake into cells
- excess lipolysis causes ketosis
- the anion gap is decreased
- total body K+ is low

Regarding the biochemistry of diabetic ketoacidosis

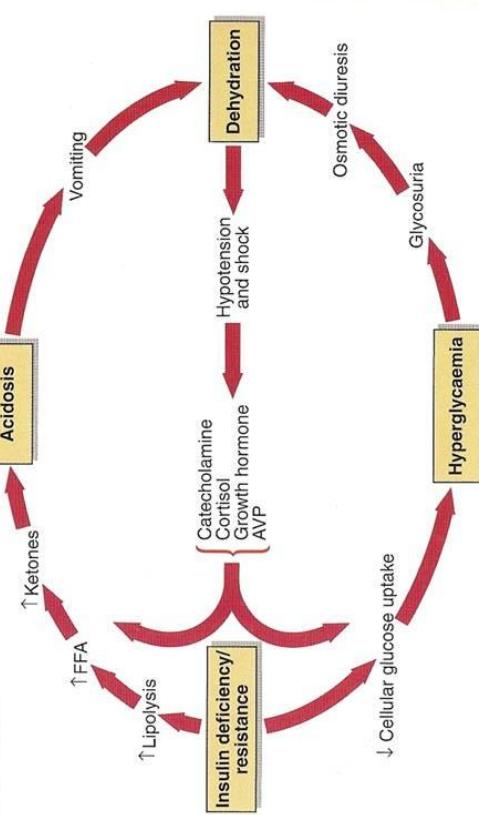


Fig. 1 The development of diabetic ketoacidosis.

Remember also HONK...

Regarding the biochemistry of diabetic ketoacidosis

- there is impaired glucose uptake into cells **T**
- excess lipolysis causes ketosis **T**
- the anion gap is decreased **F**
- total body K+ is low **T**

Regarding the biochemistry of diabetic ketoacidosis

- HONK often occurs in patients without a preceding known history of DM
- Sufficient insulin to prevent lipolysis (no ketosis)
- Very high (>30) blood glucose- last HONK I saw serum glucose 110mmol/l !! RIP..
- Very high serum osmolality (>350)
- May be trace / + ketones in urine
- Calculation of serum osmolality:

$$2(\text{Na}^+ + \text{K}^+) + \text{urea} + \text{glucose}$$
 (normal range 280-300)



Consider the following statements regarding potassium

- a. The total body potassium in a 70kg man around 3500 mmol
- b. There is normally about 4% of total body potassium in the ECF
- c. An inverse relationship exists with respect to hydrogen ions
- d. Hypokalaemia exacerbates digoxin toxicity

Hyperkalaemia

- $K > 7 \text{ mmol/l}$ requires immediate treatment
- Calcium gluconate (or chloride) \rightarrow cardioprotection
- Glucose and insulin \rightarrow redistribution of K
- Salbutamol Neb \rightarrow redistribution of K
- Sodium bicarb \rightarrow redistribution of K
- Resonium \rightarrow ion exchange with K
- $K^+ & H^+$ have a *RECI/PROCAL* relationship



Consider the following statements regarding potassium

- a. The total body potassium in a 70kg man around 3500 mmol **T**
- b. There is normally about 4% of total body potassium in the ECF **F**
- c. An inverse relationship exists with respect to hydrogen ions **F**
- d. Hypokalaemia exacerbates digoxin toxicity **T**

Regarding arterial blood gases

- a. the liver is the main organ responsible for compensatory changes to respiratory acidosis/alkalosis
- b. metabolic acidosis is associated with hyperkalaemia
- c. the normal range for base excess is +2.3 mmol/l to -2.3 mmol/l
- d. the hydrogen carbonate (HCO_3^-) is a measured value





Henderson- Hasselbach Equation...

- pH, PCO₂ and PO₂ are measured values
- Henderson- Hasselbach Equation calculates HCO₃

$$pH = 6.1 + \log \frac{HCO_3}{0.235 \times PaCO_2}$$

- important buffering mechanisms occur acutely in erythrocytes (carbon dioxide carriage) and more slowly in kidneys by HCO₃ and H⁺ excretion changes



Regarding arterial blood gases

- pH, PCO₂ and PO₂ are measured values
- the liver is the main organ responsible for compensatory changes to respiratory acidosis/alkalosis
- metabolic acidosis is associated with hyperkalaemia
- the normal range for base excess is +2.3 mmol/l to -2.3 mmol/l
- the hydrogen carbonate (HCO₃) is a measured value



Consider the following statements regarding lactate

- a. Metformin ingestion gives rise to increased lactate production
- b. Lactic acid is metabolised in both the liver and kidneys
- c. A fluoride oxalate sample tube is used to measure lactate
- d. Mesenteric ischaemia leads to a reduced serum lactate

↑LACTATE...



DECREASED METABOLISM

- Hepatic failure
- Renal failure
- Hypothermia
- Alkalosis
- Sepsis
- DM
- hereditary

INCREASED PRODUCTION

- Intravascular volume depletion
- Tissue hypoxia/ hypoperfusion
- Exercise/ seizures/ trauma
- Drugs
 - Metformin
 - Salicylates
 - Cyanide
 - COHb
 - Iron
 - isoniazid

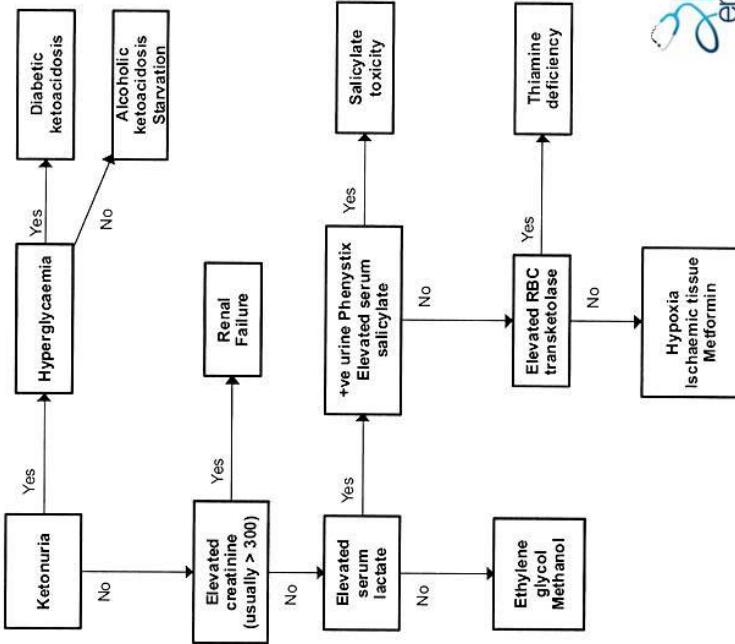
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- b. Lactic acid is metabolised in both the liver and kidneys **T**
- c. A fluoride oxalate sample tube is used to measure lactate **F**
- d. Mesenteric ischaemia leads to a reduced serum lactate **F**

The following are true with respect to the anion gap

- a. the anion gap represents the concentration of anions actually present in the plasma but which are not measured with routine chemistry
- b. the normal value of the anion gap is +5mmol/l to -5mmol/l
- c. injection of methanol gives an increased anion gap
- d. hypoalbuminaemia gives a reduced anion gap

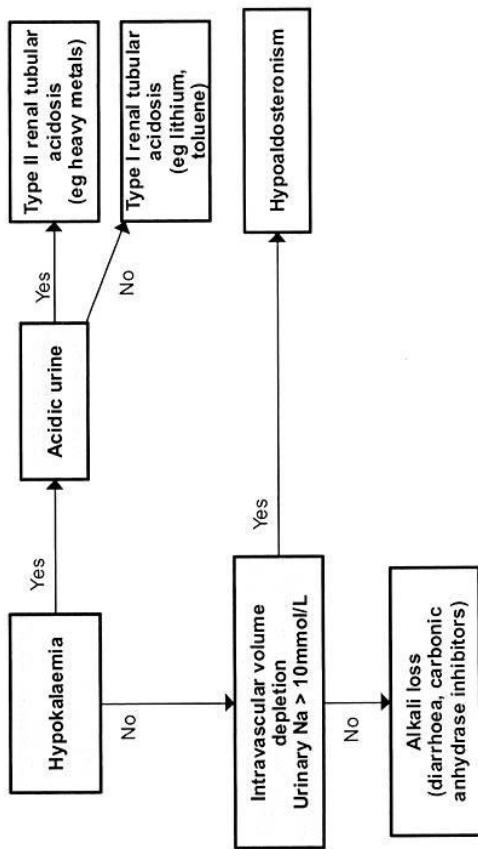
ASSESSMENT OF HIGH ANION GAP ACIDOSIS



Causes of a raised anion gap...

Methanol
Uraemia
Diabetic ketoacidosis
Paraldehyde
Isoniazid
Lactic acidosis
Ethyleneglycol or ethanol
Salicylate
 $AG = [Na^+ + K^+] - [Cl^- + HCO_3^-] \sim 8-16 \text{ mmol/L}$

ASSESSMENT OF NORMAL ANION GAP ACIDOSIS



The following are true with respect to the anion gap

- a. the anion gap represents the concentration of anions actually present in the plasma but which not measured **T**
- b. the normal value of the anion gap is +5mmol/l to -5mmol/l **F**
- c. injection of methanol gives an increased anion gap **T**
- d. hypoalbuminaemia gives a reduced anion gap **T**

Energy...

- Mitochondria are our intracellular power houses
- Aerobic pathway 1 mol glucose → 38 ATP
- Anaerobic 1 mol glucose → 2 ATP (rate of glycolysis exceeds O₂ delivery)
- If body temperature exceeds 41-42 ° C the rise in the metabolic rate fails and heat exhaustion results
- Cooling hyperthermics can be done quickly vs warming hypothermics must be done at no greater than 0.5-1 ° C/hr

Regarding energy production in the body

- a. mitochondria are the site of oxidative phosphorylation
- b. the conversion of glucose to lactate produces only 2 mol ATP per mol blood glucose
- c. the citric acid cycle has an absolute requirement for oxygen
- d. for every degree of fever above 37.0, the energy requirement of the body increases 14%



Consider the following statements regarding liver function

- a. A disproportionately raised ALT suggests biliary obstruction T
- b. A reduced prothrombin time is a sensitive indicator of liver damage F
- c. Albumin has a plasma half-life of 120 days
- d. Placental ALP appears in the maternal blood in the second trimester of pregnancy F
- e. The aminotransferases are the best indicators of paracetamol toxicity T



Regarding energy production in the body

- a. mitochondria are the site of oxidative phosphorylation T
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- c. the citric acid cycle has an absolute requirement for oxygen F
- d. for every degree of fever above 37.0, the energy requirement of the body increases 14% T



LFTs

- ↑ AST & ALT (AMINOTRANSFERASES)
 - Non-specific markers of hepatocellular injury
- ↑ ALP
 - Increased synthesis from bile canaliculi cells
 - Cholestasis
 - Also found in bone, small intestine, placenta & kidney
- ↑ GGT
 - Microsomal enzyme
 - With ↑ALP suggest ALP is of hepatic origin
 - Alcohol, phenytoin
- ↑ PROTHROMBIN TIME (INR)
 - Very short half-life; very sensitive indicator of reduced hepatic synthesis (paracetamol OD)



Consider the following statements regarding liver function

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- c. Albumin has a plasma half-life of 120 days F
- d. Placental ALP appears in the maternal blood in the second trimester of pregnancy T
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The following statements regarding the metabolic response to injury are true

- Both glycolysis and gluconeogenesis are increased
- Proteolysis is reduced overall
- The severity of the flow phase determines clinical outcome
- A body temperature of $<36^{\circ}\text{C}$ and a white blood cell count of $<4000/\text{mm}^3$ are recognised diagnostic criteria for SIRS
- Plasma albumin often rises in the first 48 hours



Metabolic response to injury...

- is a **protective physiological response**

- The severity of the **EBB phase** determines clinical outcome and may progress to recovery or to **SIRS**
- The **FLOW phase** involves changes in metabolism to ensure energy is made available to dependent tissues (**CATABOLISM**)
- The **FLOW phase** persists until the inflammatory response provides for tissue healing and/or eradication of infection (**ANABOLISM**)
- **CRP** and **ALBUMIN** are useful for monitoring



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- The severity of the flow phase determines clinical outcome **T**
- A body temperature of $<36^{\circ}\text{C}$ and a white blood cell count of $<4000/\text{mm}^3$ are recognised diagnostic criteria for SIRS **T**
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THANKS & GOOD LUCK!

- Recommended reading- *Clinical Chemistry* (Gaw, Murphy, Cowan, O'Reilly, Stewart, Shepherd)
- *Basic Medical Sciences for MRCP Part 1- Easterbrook*

Part 4

Course Evaluation

Evaluation form

MCEM Part A Course, 26th & 27th April 2014. Chennai, India.

Please insert a number from '1' (very poor) to '5' (very good) in the second column.

Topic	1- 5	Comments
Setting (room, etc)		
Catering		
Practice papers useful (as far as you are aware)		
Discussion helpful		
Good use of your time		
Would you recommend this course to others		

Presentation	1- 5	Comments
Exam & revision tips		
Microbiology		
Respiratory physiology		
Clinical questions practice		
Pathology		
Haematology		
Neuroanatomy & Physiology		
Cardiac Physiology		
Pharmacology I		
Pharmacology II		
Frequently Asked Questions		
Anatomy I		
Anatomy II		
Working in UK: MTI		
MCEM Quiz		

How did you hear about the course?

a) word of mouth b) flyer c) search engine (e.g. Google)

d) other, please specify.....

How could the course be improved?

